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SURGICAL TREATMENT OF THE PATENT DUCTUS ARTERIOSUS

Report of Five Cases

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SINCE 1907, the possibility of operation in the treatment of the patent ductus arteriosus has been recognized. Graybiel, Strieder and Boyer [1] made the first surgical attempt at closure of the ductus. The condition was complicated by the presence of bacterial endarteritis. The unsuccessful outcome was due to fatal hemorrhage at the operating table. Since this first attempt Gross [2] has ligated or divided the ductus in 133 patients with only five fatalities.

In reviewing the literature on this subject, one is impressed by the rapid advancement made in the accuracy of diagnosis and the perfection of the surgical technic. The early criteria for operation, namely, absence of infection, absence of embolic phenomena and sterile cultures of the blood no longer need be followed. The surgical treatment encompasses more and more the group of patients previously denied operation because of the presence of infection superimposed on the patent ductus.

The purpose of this paper is to add 5 cases to the literature and to discuss some problems in the preoperative and postoperative care of these patients. Each patient in this group was individual enough in the problems of therapy to warrant separate comment. The changes in therapy have more or less followed the advancement in chemotherapeutic agents and more recently the addition of biologic agents.

The literature on the subject of patent ductus arteriosus has been thoroughly summarized both from a medical and from a surgical view-

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1. Graybiel, A.; Strieder, J. W., and Boyer, N. H.: An Attempt to Obliterate the Patent Ductus Arteriosus in a Patient with Subacute Bacterial Endarteritis, Am. Heart J. **15**:621, 1938.

2. Gross, R. E.: Paper read at the Meeting of the American Association for Thoracic Surgery, Detroit, May 1946.

(Footnotes continued on next page)

point by Burch [3] and Shapiro and Keys.[4] The embryology, physiology, clinical features and laboratory findings have been fully discussed in the excellent papers of Bullock, Jones and Dolley [5] and Gross.[6] This congenital anomaly when present alone or complicated by bacterial endarteritis carries a serious prognosis. The studies of Shapiro and Keys [4] have shown the end results in cases in which the patients were untreated. Shapiro and Keys [4] have found that 86 per cent of patients with this cardiac lesion died of causes directly attributable to their heart disease. They discussed a series of 140 patients operated on, with an over-all mortality rate of 8.5 per cent in cases uncomplicated by bacterial endarteritis. Thirty-three patients in their collected series had bacterial endarteritis at the time of operation. A 50 per cent rate of cure was obtained in the infected group. These figures lead one to believe that surgical intervention for this arteriovenous fistula should be attempted whenever possible.

The indications for operation are generally listed to include the following symptoms: physical retardation, cardiac failure, cardiac embarrassment without frank failure and a patent ductus plus superimposed bacterial endarteritis. It seems that this is not inclusive enough. This anomaly is certainly one instance in which prophylactic surgical treatment could be practiced, with great benefit. By now, the published articles have demonstrated the end results in untreated patients. Operation should not be denied to patients because of fear of a surgical mortality. Their chances of normal longevity if untreated are far less than their chances if operation is done. The mortality rate of 86 per cent in untreated patients as compared with 8.5 per cent in treated patients strengthens the argument. Burch [3] stated, "the surgical risk is still too great in average hands to recommend surgery in all patients with patent ducti." Any surgeon experienced in thoracic surgery is capable of performing this operation. Once the diagnosis of this lesion has been made operation should be the treatment of choice.

Bullock, Jones and Dolley [5] and Gross [7] have shown that the younger patients are more easily handled from a technical viewpoint and the

3. Burch, G. E.: Congenital Patent Ductus Arteriosus: An Evaluation of its Surgical Treatment, M. Clin. North America **28**:388, 1944.

4. Shapiro, M. J., and Keys, A.: The Prognosis of Untreated Patent Ductus Arteriosus and the Results of Surgical Intervention: A Clinical Series of Fifty Cases and Analysis of One Hundred and Thirty-Nine Operations, Am. J. M. Sc. **206**:174, 1943.

5. Bullock, L. F.; Jones, J. E., and Dolley, F. S.: The Diagnosis and the Effects of Ligation of the Patent Ductus Arteriosus, J. Pediat. **15**:786, 1939.

6. Gross, R. E.: Surgical Closure of the Patent Ductus Arteriosus, J. Pediat. **17**:716, 1940.

7. Gross, R. E.: Complete Surgical Division of the Patent Ductus Arteriosus; A Report of Fourteen Successful Cases, Surg., Gynec. & Obst. **78**:36, 1943.

ductus easily approached and more amenable to ligation or division. Shapiro and Keys [4] have suggested that the probability of bacterial endarteritis increases with age. This further supports the plea for early surgical intervention.

The accuracy with which the diagnosis of the patent ductus arteriosus can be made is well illustrated by the work of Gross,[7] Bullock and associates [5] and others. Shapiro and Keys [4] found only two instances of mistaken diagnosis in the literature. There is no way of estimating the conditions that are wrongly diagnosed but not reported. In this series of 5 cases, the diagnosis was proved correct in all instances. Diagnosis and the preoperative preparation of these patients were entirely the work of the medical department. A great deal of credit is due them for the excellent preparation of these extremely sick patients. The results in this group of patients were dependent on their excellent physical condition prior to the operative day. In only 1 patient was there any question as to the diagnosis. Clinically the diagnosis was made by the medical staff, although the roentgenologic and laboratory studies were not confirmatory. The remaining 4 cases were clearcut in their diagnostic findings. It has been found that the history and physical examination are the most definite aids in making the diagnosis of a patent ductus arteriosus. All these patients had been told at an early age that there was something wrong with their heart. Four of the 5 patients had complications of their cardiac lesion, namely, infection, with or without emboli. Each patient presented the classic thrill over the heart, maximum to the left of the sternum in the second and third intercostal spaces, and a continuous machinery murmur with systolic accentuation in the same area. A systolic murmur at the apex of the heart was present in 4 of the 5 cases. All but 1 patient had cardiac enlargement by clinical examination. This was confirmed at the time by fluoroscopic examination. All these patients had a widened pulse pressure with a lowered diastolic pressure. Four of the 5 patients had congestion of the left lung, enlargement of the pulmonary conus and a hilar dance demonstrated by roentgenologic and fluoroscopic examination of the heart and lungs. In 3 cases septicemia was proved preoperatively with the culture of Streptococcus viridans. In 1 case bacterial endarteritis was not present. In 1 case the clinical picture of septicemia was present, with multiple pulmonary infarcts and a splenic infarct, but no organisms were grown on culture of the blood.

All 5 patients were admitted to the medical service of the North Carolina Baptist Hospital and transferred to the surgical service at the time of the operation. The youngest patient was 18 years old, and the oldest patient was 30 years. The youngest patient did not have bacterial endarteritis. It is interesting to note that with the exception of the youngest patient each patient had not only bacterial endarteritis but also

embolic accidents previous to operation. In the following paragraphs the cases are presented in chronologic order on the basis of the date of operation.

CASE 1.—The patient was a 28 year old factory worker who had had "heart trouble" all his life. Prior to the present illness the patient had always been well. It had never been necessary for him to restrict his activities. There was no history of dyspnea on exertion or orthopnea. The patient had never noticed cyanosis.

On physical examination the patient had a temperature of 102 F. His pulse rate was 110 and his blood pressure 140 systolic and 56 diastolic. Scattered petechiae were seen over the skin and mucous membranes and beneath the nail beds. The heart was enlarged to the left, and on auscultation the classic murmur and thrill of a patent ductus arteriosus were heard and felt.

Laboratory studies revealed mild secondary anemia, with a leukocytosis of 16,000. A roentgenogram of the chest showed some hilar consolidation of the left lung. The pulmonary conus was prominent, and on fluoroscopic examination a hilar dance was demonstrated. An electrocardiogram was reported as normal. Cultures of the blood the day of admission produced fifty colonies of Str. viridans per cubic centimeter. On four successive days repeated blood cultures of the blood showed the same results. On the second hospital day the patient experienced sudden, sharp pain in the right side of the chest.

On physical examination at this time a pulmonary infarct in the periphery of the lower lobe of the right lung was found. This was substantiated by the roentgenologic findings. He was given large doses of sulfanilamide by mouth; his blood sulfanilamide level was maintained at approximately 12 mg. per hundred grams. There was a definite reduction in the number of colonies of Str. viridans, but cultures of the blood never became sterile.

He was operated on, and a patent ductus arteriosus was found and doubly ligated with braided silk. His postoperative course was not remarkable. Cultures of the blood remained sterile from the day of operation. The patient was discharged on his fourteenth postoperative day, with a well healed wound and symptom free.

Comment.—This patient was operated on in the prepenicillin era. Use of the chemotherapeutic agents at hand was unsuccessful in sterilizing the blood stream. Accordingly, he was operated on in the presence of fever and bacterial endarteritis. At the time of operation the patient was malnourished, had a definite loss of weight and in general was a poor surgical risk. He is alive and well three years after operation. There is no cardiac murmur or thrill at the present time.

CASE 2.—The patient was a 25 year old mill worker, admitted because of fever, generalized malaise, weakness and loss of weight over a period of six months. A diagnosis of subacute bacterial endocarditis was made before entry.

The past history was noncontributory. He had been told as a young boy that he had a "leaking heart."

On physical examination the temperature was 103 F., pulse rate 120, respiratory rate 20 and the blood pressure 120 systolic and 40 diastolic. He presented the classic findings of a patent ductus arteriosus. There was evidence of cardiac enlargement on the right and left sides. The pulse was Corrigan in type. There were scattered petechiae over the mucous membranes. Neurologic examination suggested a cerebral embolus involving the arm and forearm centers in the right cerebral cortex.

The laboratory findings showed no anemia or leukocytosis. The sedimentation rate was 53 mm. per hour corrected. Cultures of the blood produced twenty to twenty-five colonies of Str. viridans per cubic centimeter. The electrocardiogram showed ventricular hypertrophy on the left side. The roentgenogram of the chest showed cardiac enlargement and hilar pulmonary congestion on the left side.

Sulfadiazine was given orally in doses of 6 Gm. every twenty-four hours. After several days the temperature and pulse were normal, although the cultures of the blood remained positive. Operation was advised, but the patient decided against this and left the hospital. He was readmitted six weeks later, with a return of all his symptoms. His temperature was 102 F. At this time the hemoglobin content was 60 per cent, with 3,300,000 red blood cells. Cultures of the blood remained positive for Str. viridans. He was given two small transfusions of blood to prepare him for operation. In vitro studies of the organisms in the blood showed no sensitivity to sulfadiazine, sulfathiazole or sulfapyridine, and accordingly no chemotherapy was given. The day of operation cultures of the blood produced forty-five colonies of Str. viridans per cubic centimeter. The patient had a patent ductus at operation, which was ligated doubly with heavy, braided, black silk.

This patient was admittedly a poor operative risk. He had already suffered a cerebral embolus and had had a prolonged febrile course prior to operation. The postoperative course was stormy. Although the blood stream became sterile after ligation of the patent ductus the patient progressed steadily downhill, and he died on the fourth postoperative day. Forty-eight hours postoperatively Str. viridans was again cultured from the blood stream. At autopsy numerous infarcts were found in the spleen, small bowel and cerebrum. Vegetations were present on the aortic valves, from which Str. viridans organisms were cultured. The patent ductus was firmly occluded, and the ligatures were intact.

Comment.—The presence of cerebral emboli, preoperatively, the long-standing septicemia and the positive cultures of the blood following operation all contributed to his death. Operation was done because it was believed to offer the only chance this patient had for survival. The findings at autopsy, of course, explain the reasons for the persistently positive cultures of the blood. If penicillin had been available at the time of operation, perhaps this focus on the aortic valves could have been controlled.

Case 3.—A 24 year old housewife was admitted because of weakness, malaise, loss of weight, elevated afternoon temperature and "rheumatism," of three months' duration. There had been a known cardiac lesion present since the age of 3 months. Previous to admission to the North Carolina Baptist Hospital, the patient had been treated with penicillin. A diagnosis of congenital cardiac lesion with superimposed bacterial endocarditis had been made. There had been no improvement in the general condition of the patient.

Five weeks prior to admission there developed pain in the left side of the chest, rusty sputum and spiking fever. A diagnosis of pulmonary infarction was made. The patient during this time noticed petechiae under her nail beds. The administration of penicillin was continued, without improvement, until her admission to the North Carolina Baptist Hospital.

On physical examination a temperature of 101 F., pulse rate of 104 and respiratory rate of 22 were found. The blood pressure was 94 systolic and 56 diastolic. The weight was 75 pounds (34 Kg.). Scattered petechiae were found in the buccal mucous membranes and in the nail beds. The lungs were clear, and no friction

rub was heard. The heart was enlarged to percussion. To the left of the sternum, in the second intercostal space, the classic murmur and thrill of a patent ductus arteriosus were found. The abdomen was normal except for the presence of a scar low in the midline. There was no clubbing of the extremities.

Accessory laboratory findings were a hemoglobin content of 10 Gm., with 3,100,000 red blood cells, and a white blood cell count of 17,000, with 17 per cent young polymorphonuclear leukocytes. The sedimentation rate was 47 mm. per hour corrected. Cultures of the blood produced fifty colonies of Str. viridans per cubic centimeter. Fluoroscopic examination of the chest showed the cardiac pulsations to be excessively active. There was some fulness in the region of the pulmonary conus. The sign of a hilar dance was present.

Penicillin in concentrations of 1 Oxford unit per cubic centimeter completely inhibited growth of the organisms cultured from the blood stream. With knowledge that previous penicillin therapy had been ineffectual in sterilizing the blood stream, this patient was given continuous intramuscular penicillin drips, receiving 240,000 Oxford units every twenty-four hours. Improvement was rapid. Within seventy-two hours, the temperature curve was normal and cultures of the blood were sterile. Several small transfusions were given and the patient transferred to the surgery.

At operation, a patent ductus measuring 10 mm. in length and 7 mm. in width was found. It did not prove to be abnormally friable. Visceroparietal adhesions were numerous but fine and easily freed. The ductus was divided between clamps and the ends oversewn. The chest was closed without drainage. Postoperatively the patient was afebrile after twenty-four hours, and the left lung was completely reexpanded by roentgenologic study. The patient was allowed to go home on the twelfth day. Daily cultures of the blood taken postoperatively were sterile. Penicillin was continued for twenty-four hours after operation. Six months later the patient was entirely well and had gained 25 pounds (11.3 Kg.).

Comment.—This was the first patient operated on after penicillin became available for civilian use. It was also the first time that the ductus was severed completely by us. This patient was certainly a better operative risk, probably as a result of penicillin therapy. She was operated on when free of symptoms and afebrile and in the presence of a good nutritional state. The case also illustrates the value of in vitro studies in the use of biologic agents and the ever present variable factor of blood concentrations during penicillin therapy.

CASE 4.—An 18 year old married girl had been told at the age of 12 years that she had heart trouble. One year prior to admission she was refused life insurance because of heart disease. She was constantly aware of a humming in her chest, which was greatly accentuated by activity.

Results of physical examination were entirely normal except for abnormal cardiac findings. There was a continuous machinery-like murmur in the second and third left intercostal spaces, with a systolic accentuation. There was a palpable thrill over the same area.

Accessory clinical findings showed no anemia or leukocytosis. Fluoroscopic and roentgenologic examination of the chest showed some enlargement of the heart, principally of the left ventricle. There was no enlargement of the pulmonary conus, and no hilar dance was seen.

The indication for operation of this patient was, first, the presumed presence of a patent ductus arteriosus and, second, the findings of early cardiac enlargement. At operation the ductus was found to be short and wide. It measured

less than 2 mm. in length and approximately 4 mm. in width. It was impossible to divide because of its short length. Efforts to increase its length by subadventitial dissection, as proposed by Touroff,[8] were not successful. In addition the patient presented a saccular aneurysm of the pulmonary artery proximal to the patent ductus. Four plicating sutures of no. 00000 waxed arterial silk were used to occlude the lumen. This obliterated the murmur.

This case represented the only instance of the posterolateral approach to the ductus, as recommended by Harrington.[9] The reason for using this approach was that this girl had large pendulous breasts and incision above or below the mammary gland would have required extensive dissection.

The patient's chest was closed without drainage. Her postoperative course was uneventful. She was discharged from the hospital on her ninth postoperative day. At present, six months later, she is symptom free. On examination, however, there was a distant soft murmur at the second left interspace. Whether this represents a recurrence or a murmur associated with the pulmonary aneurysm found at operation is not known. Such murmurs have been heard at the operating table after the ductus has been completely severed and are presumably due to a swirling of blood in the stump of the ductus on the pulmonary end.

Comment.—This case illustrates the variable pathologic conditions found in any group of congenital cardiac lesions. It will take time to tell whether or not this patient was benefitted by operation.

CASE 5.—A 30 year old housewife was admitted with complaints of diarrhea, fever and chills of seven weeks' duration. There had also been considerable cough, blood-streaked sputum and thoracic pain. Her health prior to this time had been good.

Her past history was that she had been treated for "ulcer of the stomach" for five years. She had never been incapacitated by this lesion and carried on her work without difficulty.

On physical examination the temperature was 103 F., pulse rate 120 and respiratory rate 20. The blood pressure was 120 systolic and 70 diastolic. She presented the typical thrill and murmur of a patent ductus arteriosus. There were changes in the left pulmonary field and pleura compatible with pulmonary infarction. Examination of the abdomen was noncontributory. There was no clubbing or cyanosis of the extremities.

The accessory laboratory findings were not remarkable. Roentgenograms of the chest showed areas of fibrosis in the periphery of both pulmonary fields, which were interpreted as being healed pulmonary infarcts. The pulmonary conus was enlarged, and the hilar dance was present. A series of roentgenograms of the gastrointestinal tract showed a healing duodenal ulcer, without obstruction. Repeated cultures of the blood were sterile. Agglutinations for typhoid and paratyphoid fever gave negative results.

In spite of sterile cultures of the blood it was felt that this patient had bacterial endarteritis superimposed on a patent ductus arteriosus. She was given penicillin, 20,000 Oxford units intramuscularly every three hours. This was increased to

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8. Touroff, A. S. W.: The Results of Surgical Treatment of Patency of the Ductus Arteriosus Complicated by Subacute Bacterial Endarteritis, Am. Heart J. **25**:187, 1943.

9. Harrington, S. W.: Patent Ductus Arteriosus with Bacterial Endarteritis: Transpleural Ligation Through Posterolateral Approach: Report of a Case, Proc. Staff Meet., Mayo Clin. **18**:217, 1943.

60,000 units every three hours when she failed to improve clinically on the smaller dose. Her temperature returned to normal, and there was striking subjective improvement. During her stay in the hospital she was given aluminum hydroxide gel and tincture of belladonna to control her ulcer, along with a special diet. She asked release from the hospital at Christmas and returned to the hospital after the holiday for operation. At home a daily temperature chart showed no elevation of temperature.

She was readmitted for operation. The patent ductus was the largest in this series, measuring 15 mm. in length and 11 mm. in width. It was easily divided between clamps and the ends oversewn with fine, black, waxed silk.

Her postoperative course was uneventful. She was discharged afebrile and generally improved on her tenth postoperative day. The murmur has not recurred, nor has she had recurrence of fever. She is well six months after operation. The causative organisms were never proved in this case.

Comment.—This case was puzzling from a bacteriologic standpoint, because it was never possible to demonstrate organisms in the blood stream in spite of a clinical picture of septicemia. Her response to penicillin was certainly suggestive of septicemia and the postoperative result seemed conclusive.

COMMENT

The use of penicillin in the treatment of bacterial endarteritis is not new. The more recent medical literature contains reports of successful treatment of this disease with penicillin. To date there has been nothing reported in the surgical literature about the use of penicillin in the treatment of the patent ductus with superimposed bacterial endarteritis prior to the surgical intervention of this fistula. The course of patients treated with penicillin has been impressive compared with that of those operated on with positive cultures of the blood and no penicillin. Certainly a large series will most likely show more failures, but when in vitro studies show organisms in the blood stream sensitive to penicillin its use should constitute the primary goal of preoperative preparation.

Touroff [10] in 1942 advised early ligation in the cases of patent ductus with infection. He stated that chemotherapy is of no help in controlling the disease process. This viewpoint must be altered with the advent of penicillin. One case in this group illustrates the variability of penicillin therapy. How much penicillin and how long it is to be given must be determined by the clinical course of the patient.

The patients in the first 2 cases perhaps have been greatly benefited by preoperative sterilization of the blood stream. A patient with loss of weight, fever and septicemia presents alone a formidable surgical risk. Certainly it is desirable to have these patients in the best of physical condition before surgical treatment of the patent ductus is attempted. Gross [7] suggested that patients who were proved to have embolic acci-

10. Touroff, A. S. W.: Further Experiences in the Surgical Treatment of Subacute Streptococcus Viridans Endarteritis Superimposed on Patent Ductus Arteriosus, J. Thoracic Surg. **12**:1, 1942.

dents were poor surgical risks and should not be subjected to operation. Touroff [8] stated the belief that this does not contraindicate operation. He reported 4 cases in 1943 with successful recovery following surgical ligation of the patent ductus. All his patients had embolic accidents prior to operation. This report adds 3 cases to this group. The use of penicillin will help reduce the mortality rate, and thus operation can be offered to that group of patients denied surgical treatment because of the risk. This small group of patients suggests that there is some advantage to penicillin therapy. More operations must be done before any definite conclusions can be made.

The operative procedures have been standardized by Gross.[7] The procedure in this group is essentially the same. Four of the 5 patients were operated on through an anterior incision, with subperiosteal resection of the anterior two thirds of the costal cartilage and rib. One patient was operated on through the posterolateral approach, as recommended by Harrington.[9] There were 2 men and 3 women in this series. The opinion that incision above the breast will destroy a major portion of the blood supply and lead to atrophy of the breast may not be well founded. Numerous pneumonectomies have been performed through a similar anterior incision without much difficulty; however, most of these patients were in the older age group. There has been no instance of atrophy of the female or male breast from such an incision. Review of the anatomy of this region reveals adequate circulation laterally and from below to supply the mammary tissue. None of these patients complained of numbness in the breast. Nixon [11] recommended intercostal incision without rib resection for exposure of the patent ductus. We have not used the intercostal incision.

The ductus was doubly ligated in the first 2 cases, severed between clamps and the ends oversewn in 2 cases and plicated in 1 case. It is obvious that division of the patent ductus should be the procedure of choice when possible. Ligation in continuity is simpler and certainly safer but does not absolutely rule out the possibility of recurrence. A satisfactory clamp which is dependable has not been advised. At present such a clamp is being made, which it is hoped will be satisfactory. The patent ductus is so variable in size that no uniform method of division or ligation can be anticipated. Of the 5 cases 1 could have been ligated as suggested by Blalock.[12] Cellephane or sclerosing agents injected between ligatures has not been used in any of these patients.

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11. Nixon, J. N.: Surgical Closure of the Patent Ductus Arteriosus, Texas State J. Med. **40**:473, 1945.

12. Blalock, A.: Operative Closure of the Patent Arteriosus, Surg., Gynec. & Obst. **82**:113, 1946.

In the group of patients with bacterial endarteritis the ductus varied in length and width, but in none was it excessively friable. It should be noted that the 2 cases in which the ductus was divided between clamps represented cases complicated by bacterial endarteritis.

The mediastinal pleura was closed in the last 3 cases, since it was felt that the area was sterile due to the penicillin therapy. Mediastinitis was thus not feared. The chest was closed without drainage. The air in the pleural space was removed by catheter suction through a catheter left in the pleural space during closure. This was removed after the thoracic incision was completely closed. Although 4 of the 5 patients had previous pulmonary infarcts, visceroparietal pleural adhesions were never a great problem.

SUMMARY

Five patients were operated on with ligation or division of the patent ductus arteriosus. There was one death in this group. Four of the 5 patients had subacute bacterial endarteritis complicating their congenital cardiac disease. These same 4 patients had preoperative embolic accidents, the chief site being the lung. Penicillin was satisfactorily used in controlling the septicemia in the last few patients.

CONCLUSIONS

Penicillin has materially aided in reducing the mortality rate of patients with subacute bacterial endocarditis superimposed on a congenital patent ductus arteriosus.

The severance of the patent ductus is preferable to ligation in continuity when possible.

The anterior approach to the mediastinum, with rib resection, has proved satisfactory.

The patent ductus arteriosus should be corrected more frequently when found.

Embolic accidents do not usually contraindicate operation for the patent ductus arteriosus.

LYMPHOGRANULOMATOUS STRICTURES OF THE RECTUM

A Résumé of Four Hundred and Seventy-Six Cases

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LYMPHOGRANULOMA venereum and particularly strictures of the rectum caused by this disease have been the subject of many reports in recent years. It is generally recognized that the anorectal manifestations of this widespread disease offer the most serious threat to life and are, likewise, most difficult to treat satisfactorily. At Harlem Hospital we have had an opportunity to study a large number of cases of fibrous inflammatory strictures of the rectum, and this paper is a study of 476 consecutive cases in which patients were admitted to the wards of the hospital during the fifteen and a half year period from Jan. 1, 1930, to Aug. 1, 1945. The more attention we have given this disease, the more we have come to realize that our knowledge is still extremely incomplete and that increased clinical and laboratory study is needed to clear up many aspects of the subject. Some clinical aspects of this disease have been treated by members of the staff of this hospital in previous papers.[1]

HISTORICAL SUMMARY

Brief mention should be made of the early history of this important and increasingly interesting disease and its rectal manifestations.

As early as 1824 Martland,[2] a Scottish surgeon, performed an iliac colostomy on the left side, for obstruction due to a stricture, and his patient lived for seventeen years.

From the Surgical Service of Harlem Hospital, Dr. Louis T. Wright, Director.

1. (*a*) Kassebohm, F. A., and Schreiber, M. J.: Spontaneous Delivery Complicated by Rectal Stricture, Rectovaginal Fistula and Rupture of the Rectum, Am. J. Obst. & Gynec. **31**:674 (April) 1936; (*b*) Management of Labor Complicated by Rectal Stricture, New York State J. Med. **37**:484 (March 1) 1937. (*c*) Wright, L. T., and Logan, M.: Osseous Changes Associated with Lymphogranuloma Venereum, Arch. Surg. **39**:108 (July) 1939. (*d*) Levy, J. G.; Holder, E. C., and Bullowa, J. G. M.: Stricture of the Rectum Due to Lymphogranuloma Venereum: Symptoms and Treatment with Sodium Sulfanilyl Sulfanilate, Am. J. Digest. Dis. **9**:237 (July) 1942. (*e*) Wright, L. T.; Berg, B. N.; Bolden, J. V., and Freeman, W. A.: Rectal Strictures Due to Lymphogranuloma Venereum

(Footnotes continued on next page)

Hugier,[3] in 1848, was the first to describe an eroding phagedenic elephantiasis of the vulva, often accompanied with ulceration of the perineum, anus and lower part of the rectum, which he thought was due to tuberculosis, and he named it "esthiomene."

One year later, in 1849, Larsen,[4] a Danish surgeon, described rectal stricture in 11 women.

The first external rectotomy operation for rectal stricture was performed by Humphry[5] in 1856, and he stated that results in 2 of his cases were successful. This operation was reintroduced to the medical profession in 1872 by Verneuil.[6]

Gläser[7] reported the first excision operation for stricture of the rectum, in 1864. In 1867 Gläser performed a lumbar colostomy of the left side on this same patient because of intestinal obstruction due to the stricture which he had already excised and which had recurred. Twenty years later, in 1887, he did an autopsy on the same patient and found that the pelvic colon and rectum had been reduced to nothing more than a long, narrow fibrous cord perforated by a small canal, which would admit only the smallest sounds and was surrounded by inflammatory tissue.

Curling[8] was the first American surgeon to perform a lumbar colostomy for obstruction due to an incurable stricture, in 1865.

In 1875, Fournier,[9] the famous French syphilologist, described strictures of the rectum, with great accuracy, and stated that they were caused by syphilis; this was due to the fact that most of the patients

with Especial Reference to Pauchet's Excision Operation, Surg., Gynec. & Obst. **82**:449 (April) 1946.

2. Martland, R.: A Case, Edinburgh M. & S. J. **24**:271, 1825; cited by Tuttle.[11]

3. Hugier, P. C.: Memoire sur l'esthiomene ou dartre rongeante de la vulvoanale, Mém. Acad. de méd. **14**:501, 1848; cited by Nelson, N. A., in Virus and Rickettsial Diseases, Cambridge, Mass., Harvard University Press, 1940, p. 365.

4. Larsen, S. J.: Praktiske bemaerkinger over stricturer i masttarmen, Hosp.-Medd. **2**:289, 1849; cited by Jersild, O.: Notice historique sur l'infiltration hyperplasique du rectum avec rétrécissement fibreux et sur l'origine prétendue syphilitique de cette affection, Ann. de dermat. et syph. **7**:74 (Feb.) 1926.

5. Humphry, G. M.: Three Cases of Stricture of the Rectum, Treated by Incision, Assoc. M. J., London, 1856, p. 21; cited by Hartmann.[10]

6. Verneuil: Rétrécissements du rectum; traitement par la rectotomie verticale, Bull. Soc. de chir. de Paris **1**:447, 1872; cited by Hartmann.[10]

7. Gläser, J. A.: Stricture des Mastdarmes mit Mastdarm-Scheidenfistel, Arch. f. klin. Chir. **9**:509, 1868; **34**:459, 1887; cited by Hartmann[10] and by Tuttle.[11]

8. Curling, T. B.: Correspondence, Am. J. M. Sc. **91**:575, 1873; cited by Tuttle.[11]

9. Fournier, A.: Lésions tertiares de l'anus et du rectum, Paris, A. Delahay, 1875.

who showed the disease also had coexistent syphilis, and he termed the condition "anorectal syphiloma."

Henri Hartmann,[10] of Paris, was the first surgeon to comprehend the disease fully. He performed sixteen external rectotomy operations, with unsuccessful results, early in his career, and in 1895 he reported thirty-five excision operations with successful results. In 1930 he made a report of sixty-six excision operations for rectal stricture. He wrote many articles on the subject and reported numerous clinical histories of cases, which represent the best clinical study of rectal strictures that has been published, and this in spite of the fact that he knew nothing about the Frei test, the true etiologic agent or the systemic nature of the disease. Hartmann had careful histopathologic studies made of all specimens removed at operation, and the pathologic work of M. Toupet was exceptionally detailed and thorough.

Tuttle,[11] in this country, in 1902, described rectal strictures, with great accuracy, although he, like Fournier and Hartmann, did not know their true cause and therefore employed the generic term "inflammatory strictures." Tuttle did not enter into the field of active controversy as to whether these strictures were due to gonorrhea, syphilis or tuberculosis, but he did state unequivocally that all these strictures were preceded by ulceration.

Two contributions stimulated great interest in this disease, namely, the description by Durand, Nicolas and Favre,[12] of Lyons, in 1913, of the disease as a distinct clinical entity and the introduction by Wilhelm Frei [13] of his intracutaneous test. This interest has continued up to the present time.

Frei and Koppel,[14] in 1926, brought forward evidence that proved that the occurrence of benign strictures of the rectum and elephantiasis of the genitals was of lymphogranulomatous origin, by means of Frei's intradermal test. Their work was confirmed by Bensaude and

10. Hartmann, H.: Chirurgie du rectum, Paris, Masson & Cie, 1931, p. 166; L'extirpation des rétrécissements inflammatoires du rectum, Bull. et mém. Soc. nat. de chir. **56**:855 (June 28) 1930.

11. Tuttle, J. P.: Diseases of Anus, Rectum and Pelvic Colon, New York, D. Appleton and Company, 1903, p. 463.

12. Durand; Nicolas, J., and Favre: Lymphogranulomatose inguinale subaigue, Bull. et mém. Soc. méd. d. hôp. de Paris **35**:274 (Jan. 31) 1913.

13. Frei, W.: Eine neue Hautreaktion bei Lymphogranuloma inguinale, Klin. Wchnschr. **4**:2148 (Nov. 5) 1925; Die Elephantiasis genito-anorectalis (Esthiomène und entzündliche Rektumstriktur); Eine Teilkrankheit der Lymphogranulomatosis inguinalis, Ergebn. d. ges. Med. **21**:113, 1936; Venereal Lymphogranuloma, J. A. M. A. **110**:1653 (May 14) 1938.

14. Frei, W., and Koppel, A.: Ulcus vulvae chronicum elephantiasticum (Esthiomene) und sogenanntes Syphilome anorectal als Folgeerscheinungen der Lymphogranulomatosis inguinalis, Klin. Wchnschr. **7**:2331 (Dec. 2) 1928.

Lambling.[15] Hellerstrom and Wassen,[16] in 1930, by means of intracerebral inoculation of monkeys, proved that the disease was due to a filtrable virus. Their work has been amply proved by innumerable workers throughout the world. Today the virus is demonstrable microscopically and can be grown on chick embryo mediums.

The disease has also been found to be worldwide in its distribution.

Although the early manifestations of this disease are not within the scope of this paper, it has been shown that the genitalia, anorectal region, eyes, mouth, pharynx, larynx, cervical glands, female urethra, male urethra, colon, ileum, ovaries, fallopian tubes, meninges, intra-abdominal glands, joints and bones may be involved.

TABLE 1.—*Incidence of Rectal Strictures as Regards Race and Sex*

Author	Cases, No.	White		Negro		Men		Women	
		No.	%	No.	%	No.	%	No.	%
Alley, R. C.: Tr. Am. Proct. Soc. **35**: 150, 1934	20	2	10	18	90	3	15	17	85
Mathewson, C., Jr.: J. A. M. A. **110**: 709, 1938	78	66	84.6	12	15.4	60	76.9	18	23.1
Grace, A. W.: J. A. M. A. **122**: 74, 1943 (strictures with proctitis)	90	..	....	..	....	35	36.7	57	63.3
Torpin, R.; Greenblatt, R. B.; Pund, E. R., and Sanderson, E. S.: Am. J. Surg. **43**: 688, 1939	96	4	4.2	92	95.8	0		96	100
Spiesman, M. G.; Levy, R. C., and Brotman, D. M.: Am. J. Digest. & Nutrition **3**: 931, 1937	115	11	10	104	90	12	10	103	90
Bensaude and Lambling [15]	158	..	....	..	....	70	44.3	88	55.7
Hayes, H. T.: Am. J. Surg. **16**: 323, 1932	160	..	19	..	80	..	15.8	..	84.2
Woods, F. M., and Hanlon, C. R.: Ann. Surg. **120**: 598, 1944	192	..	15	..	85	(Ratio: 7 women to 1 man)			
David, V. C., and Loring, M.: J. A. M. A.: **106**: 1875, 1936	200	..	....	Majority		..	....	Majority	
Martin, C. F.: J. A. M. A. **101**: 1550, 1933	227	..	18.4	..	81.6	0		227	100
Wright, Freeman and Bolden	476	23	4.8	453	95.2	42	8.8	437	91.2

In table 1 is listed the incidence of rectal strictures as regards race and sex by authors who have reported large series of cases.

It is seen that in this country strictures occur largely in women, particularly Negro women, and, in men, in white pederasts. Mathewson, San Francisco, reported a predominance of the disease in white persons, but his report is the one exception. The predominant frequency of rectal stenosis in women as contrasted with that in men is due to the

15. Bensaude, R., and Lambling, A., in Discussion on the Etiology and Treatment of Fibrous Stricture of the Rectum (Including Lymphogranuloma Inguinale), Proc. Roy. Soc. Med. **29**:1441 (Sept.) 1936.

16. Hellerstrom, S., and Wassen, E.: Etude du virus de la lymphogranulomatose inguinale (maladie de Nicolas-Favre), Compt. rend. Soc. de biol. **106**: 802, 1931.

difference in the lymphatic drainage. Most authors agree that stricture of the rectum in men occurs only as a result of sodomy. David and Loring are of the opinion that infection occurs in women from vaginal secretion and in men by perverted habits. Frei was of the opinion that in women sodomy was the chief cause, but with this opinion we do not agree. It is true that these conditions occur to a large extent in prostitutes and women of the lowest social strata, and is likewise a fact that many of these patients have coexisting venereal diseases, but not always. Because of the low socioeconomic status of these patients, they are to be found mainly in city hospitals. It is possible that because they belong to the lowest income group it was not until a few years ago that they began to receive intelligent and intensive scientific study, but we do know that the disease is commonest among extremely poor and illiterate persons who do not practice adequate personal hygiene and among those to whom venereal prophylaxis is unknown.

TABLE 2.—*Age Incidence*

Age, Yr.	Cases, No.
20-30	165
30-40	212
40-50	65
50-60	28
60-70	4
70-80	1
80-90	1
Total	476

Rosser [17] explained the frequency of rectal stricture in Negro women as being due to a fibroblastic diathesis of pigmented peoples and their greater tendency toward formation of scar tissue. Rosser's theory does not stand up, because of the great frequency of rectal strictures in white men who practice passive pederasty. It is a common fact that any irritating stimulus will produce a greater reaction of the fibrous tissue, such as keloids, in Negro people generally, but, nevertheless, to advance such a theory is an oversimplification of a complex problem.

In table 2 is listed the age incidence in this series of cases.

The youngest patient was 20 years and the oldest 83. It is to be noted from table 2 that the largest number of patients showing strictures of the rectum is between 30 and 40 years of age and the next largest number is between the ages of 20 and 30. This is due to the chronicity of the disease, because strictures requiring hospitalization as a rule do not develop until some years after the primary infection has

17. Rosser, C.: Proctologic Peculiarities of the Negro—The Fibroplastic Diathesis, Am. J. Surg. **37**:265 (Nov.) 1932; Benign Stricture of the Rectum, Texas State J. Med. **27**:777 (March) 1932.

occurred. Death from other concomitant diseases lessens its frequency in the later decades of life.

ETIOLOGY

The causative agent of the disease is a filtrable virus, which can be cultivated on chick embryo mediums. In their early work, Ravaut, Levaditi, Lambling and Cachera [18] inoculated monkeys with material from a patient with proliferous proctitis, and in the monkeys a typical encephalitis developed; in a second case, Laederich, Levaditi, Mamou and Beauchesne [19] produced a typical encephalitis in an ape which was inoculated with an emulsion from an adenopathic ganglion which had been produced in a guinea pig by implantation of a fragment of rectal mucosa from the patient.

Rodanische,[20] by experiments with cross immunization, indicated that there were seven strains of the virus, and, subsequently, Palmer, Kirsner and Rodaniche [21] identified five strains of the virus from material studied by them. These observers demonstrated the presence of the virus in rectal strictures in the rectal mucosa by biopsy in 4 cases; 1 patient had had a stricture for six years, 1 for eight, 1 for thirteen and 1 for twenty-one years, as judged by the onset of symptoms.

Coutts [22] stated that the virus is primarily an inhabitant of the mouth, and he attributed the growth of the disease to a growth in sexual perversion. Coutts, Martini and Landa [23] have postulated the existence of two viruses, which may be termed A and B. Virus A, they were of the opinion, produces inguinal adenitis, esthiomene vulvae, elephantiasis of the penis and scrotum and rectal stricture. Virus B is blamed for the constitutional symptoms, generalized lymphadenopathy, cutaneous changes and arthritis.

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18. Ravaut, P.; Levaditi, C.; Lambling, A., and Cachera, R.: La présence du virus de la maladie de Nicolas-Favre dans les lésions d'un malade atteint d'ano-rectite ulcéro-végétante, Bull. Acad. de méd., Paris **107**:98 (Jan. 19) 1932; cited by Stannus, H. S.: A Sixth Venereal Disease, Baltimore, William Wood & Company, 1933.

19. Laederich, L.; Levaditi, C.; Mamou, H., and Beauchesne, H.: Rétrécissement inflammatoire du rectum, forme aberrante de la maladie de Nicolas-Favre, Bull. et mém. Soc. méd. d. hôp. de Paris **48**:1072 (July 4) 1932.

20. Rodaniche, E. C., cited by Palmer, Kirsner and Rodaniche.[21]

21. Palmer, W. L.; Kirsner, J. B., and Rodaniche, E. C.: Lymphogranuloma Venereum Infection of the Rectum, J. A. M. A. **118**:517 (Feb. 14) 1942.

22. Coutts, W. E.: Glossitis marginata in ihrer Beziehung zur Lymphogranulomatosis inguinalis, Dermat. Wchnschr. **97**:1664 (Nov. 25) 1933; cited by David, V. C., and Loring, M.: Extragenital Lesions of Lymphogranuloma Inguinale, J. A. M. A. **106**:1875 (May 30) 1936.

23. Coutts, W. E.; Martini, J., and Landa, F.: Lymphogranulomatosis Venera, Am. J. Surg. **22**:96 (Oct.) 1933.

PATHOGENESIS

Primary infection, as noted by Frei, David and Loring and Grace, may in men take place directly in the rectum by pederasty, and in women the primary infection takes place in the vagina or cervix, the lymphatic vessels of which drain directly into the perirectal or pelvic glands.

The so-called Jersild syndrome, which is elephantiasis genitoanorectale, is named after Jersild,[24] who regarded rectal lesions as secondary to adenopathy of Gerota's ganglion and who stated that this results in perirectal lymphostasis.

Intensive study of the lymphatic drainage in the genital and anal regions has helped to clarify our knowledge as to how rectal strictures and associated lesions develop.

Gerota,[25] while working in Waldeyer's laboratory in Berlin, Germany, found that the anogenitoinguinal lymphatic system communicates with the rectum by multiple anastomoses and that in the lateral wall of the rectum, in all the tunica muscularis between the latter and the fascia rectipropria, immediately above the insertion of the levator ani, there are six to eight lymph glands, which receive the lymph from the lower portion of the rectum. These glands are now called the anorectal glands of Gerota.

Nesselrod[26] demonstrated that in women the lymphatic drainage from the external genitalia is inguinal, as in men, but that the drainage from the vagina and cervix is pelvic.

Barthels and Biberstein,[27] in a discussion of the genital lymphatic system, have produced data to show that the superficial lymphatic network of the vulva goes to the superficial inguinal glands and that the abundant network of the clitoris passes to the deep inguinal nodes and a few of these directly to the external iliac and hypogastric nodes. The posterior part of the vulva has, in addition, direct lymph pathways to the anal network of glands, which drain partly into the inguinal glands, partly into the anorectal glands and partly, omitting these glands, directly to the sacral lymph nodes. The lymph vessels of the lower third of the vagina, like those of the middle and upper portions, pass

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24. Jersild, O.: Les intradermo-réactions dans le chancre mou et dans la lymphogranulomatose inguinale considérées spécialement dans leurs rapports avec l'étiologie du syphilome ano-rectal, Ann. de dermat. et syph. **1**:577 (June 30) 1930; Considérations sur l'intra-épidermo-inoculation de M. Ravaut, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **38**:563 (April) 1931.

25. Gerota, D.: Die Lymphgefässe des Rektums und des Anus, Arch. f. Anat. u. Physiol., 1895, p. 240; cited by Bloom.[30]

26. Nesselrod, J. P.: Demonstration of Genito-Ano-Rectal Lymphatics, Tr. Am. Proct. Soc. **36**:85, 1935.

27. Barthels, C., and Biberstein, H.: Zur Aetiologie der "entzündlichen" Rektumstrikturen (Lymphogranulomatosis inguinalis als Grandkrankheit), Beitr. z. klin. Chir. **152**:161, 1931; cited by Bloom.[30]

mainly to the iliac and hypogastric glands, while some pass directly to the anorectal glands. The lymph vessels of the uterus go directly to the preaortic and sacral glands. Lymph glands which leave the rectal wall above the insertion of the peritoneum flow to the mesorectal lymph glands and to the glands of Gerota. Many lymph vessels lead posteriorly through the fascia of the rectum to the rectal wall, to the anorectal glands of Gerota or to the superior hemorrhoidal vessel. Lee and Staley [28] have two excellent drawings modified from Barthels and Biberstein illustrating the lymph pathways. Barthels and Biberstein have pointed out that the virus of lymphogranuloma venereum is able to produce a proliferation stimulus in the surrounding tissues.

Roegholt [29] has shown that in women there are few anastomoses between the right and left sides and between the superficial and deep lymphatic vessels; he noted that chronic lymphostasis leads to a disturbance in nutrition in the affected regions.

Bloom,[30] in his splendid review of the literature, concluded that obstruction of the lymph pathways leading to the inguinal glands causes a diversion of the lymph stream toward the rectum, and thus the infection is shunted to Gerota's glands.

Fischer and Schmidt-La Baume [31] considered that stricture results in women from infection of the vaginal mucosa, because the deep and posterior sections of the vagina send lymph into the ramified network of the pelvic lymph glands in the adipose tissue behind the rectum upward along the superior vessels and laterally along the middle hemorrhoidal vessels into a group of glands at the bifurcation of the iliac arteries.

Schreiner-Beinert [32] was of the opinion that women are more susceptible to inflammatory strictures, owing to the fact that conditions in the female pelvis are more favorable for infections normally because of menstruation, pregnancy and trauma resulting from childbirth. He stated that women have a greater tendency to ulcers in the rectum due to impacted feces in cases of constipation, and he also pointed out that in women there is a connection between the vaginal plexus and the hemorrhoidal plexus through the pudendal veins, so that infectious material usually passes from the vulva to the rectum.

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28. Lee, H., and Staley, R. W.: Inflammatory Strictures of the Rectum and Their Relation to Lymphogranuloma Inguinale, Ann. Surg. **100**:486 (Sept.) 1934.

29. Roegholt, M. N.: Das genito-rectale Syndrom, Klin. Wchnschr. **8**:1084 (June 4) 1929; cited by Bloom.[30]

30. Bloom, D.: Strictures of the Rectum Due to Lymphogranuloma Inguinale, Surg., Gynec. & Obst. **58**:827 (May) 1934.

31. Fischer, A. W., and Schmidt-La Baume: Rektalstrikturen und Lymphogranuloma inguinale, Deutsche med. Wchnschr. **58**:527 (April 1) 1932.

32. Schreiner-Beinert: Ueber entzündliche Strikturen des Rektums, Deutsche Ztschr. f. Chir. **228**:105, 1930.

Trauma during coition has been stated by some to be one of the predisposing factors in the production of rectal strictures, and it probably is a minor factor in cases in which there is a pronounced malproportion between the size of the penis and that of the vagina; unusually vigorous coitus, according to the tilt of the female pelvis, may produce in some cases irritation of the rectum through the rectovaginal septum, at the site where strictures are most commonly found. Trauma during childbirth, however, cannot seriously be considered a major causative factor, because rectal stricture in the absence of lymphogranulomatous infection is unknown among multiparous Negro women, although they do have as a racial group a greater tendency toward keloid formation than other races.

Feilchenfeld [33] stated that "genito-rectal elephantiasis can be sufficiently explained by the changes in the lymph system, but for rectal strictures, local ulceration and formation of scars must be adduced. The cause of all these changes is the virus of lymphogranulomatosis inguinale."

Most authors are of the opinion that a determining factor in the production of rectal strictures is a resultant disturbance in the lymphatic flow produced by the infection.

From the foregoing and our own observations it is reasonably clear that lymphostasis plays an important part in the pathogenesis of rectal strictures in three ways: (1) blockage of lymph glands and interference with adequate drainage; (2) involvement of the lymph channels themselves, due to the action of the virus, and (3) a specific scar tissue–producing action of the virus. Sufficient evidence has not yet been produced as to why the condition in some instances is progressive to the point where it threatens life itself; in other instances why it progresses up to the point where it becomes a serious clinical problem of importance but ceases to progress beyond this point and, finally, why in some instances it is a relatively benign chronic disease. Our opinion is that these features can be explained, in the light of our present knowledge, only on the basis of the action of different strains of the virus and the reaction of the particular host. Thus it appears that one strain of the virus may be extremely pathogenic and another strain relatively benign. Unquestionably, in many persons infected with the virus clinically important manifestations of the disease never develop. On the other hand, the disease may develop in a person, produce a rectal stricture up to a certain point and never go beyond that point, and all signs of the progression of the disease spontaneously cease. In other instances the disease progresses, and in spite of all known methods of

33. Feilchenfeld, H.: Zur Aetiologie der Elephantiasis vulvae, ano-rectalis mit den Rectumstrikturen unter besonderer Berücksichtigung der Lymphogranulomatosis inguinalis, Med. Klin. **28**:965 (July 8) 1932.

treatment this progress is continued and ultimately produces death. The complex reactions involved between different strains of the virus and the immunity reactions of the host are facts still to be elucidated.

PATHOLOGY

The stricture is usually cylindric in shape, and its length varies. Oftenest it is located 2 to 4 cm. above the anus, and its length varies from 1 to 5 cm. Hartmann found the stricture in four instances 8 to 9 cm. from the anus, and he found two coexisting strictures, one at 4 and one at 12 cm. above the anus. Ordinarily it appears as a sort of funnel, with the opening at the apex of the funnel, and the opening varies in size. On proctoscopic examination ulceration may be noticed on the surface of the stricture. At the point of stricture the rectal wall is usually grayish in appearance and rigid, if the stricture is well advanced, while in the early stages it exhibits reddened granulomatous patches and often congestion and edema.

Gosselin [34] and, later, Fournier have described an ulceration above the stricture, which spreads circularly around the rectum and extends upward from 5 to 10 cm. and over. Above this ulceration the mucosa takes on a normal appearance. The rectal wall is thickened at the point of stricture, and all its coverings are blended into a scleroedematous mass which involves the muscular layer; ofttimes there is a great amount of scar tissue external to the muscularis. Sometimes there is a lipofibrosclerotic change in all the walls of the rectum. Fissures and condylomas around the anus are common. Perianal fistulas are not unusual. Often they extend into the vagina or the vulva. Microscopically, the muscularis undergoes degeneration and becomes replaced by scar tissue, a subacute inflammatory process, which, according to Renard, one of Hartmann's pathologists, spreads between the normal elements of the tissue, following the vascular and lymphatic systems, compressing and destroying them. Masses of purulent exudate are present, with polynuclear leukocytes, debris of epithelial cells, red cells and clusters of bacteria. The submucosa is destroyed, and in it one finds round cell infiltrations. Deeper there are areas of round cell infiltrations, groups of polynuclear leukocytes, eosinophils, mast cells and many plasma cells. Nodular masses, which are often felt on palpation, are composed chiefly of round cells and have a center which often softens and takes on all the appearance of tuberculosis. Palisade formation is not unusual, and this feature is used by most modern pathologists as a basis of diagnosis. In short, the appearance is that of a chronic granuloma of the rectum, which for a long time was considered to be tuberculous or syphilitic.

34. Gosselin, L.: Recherches sur les rétrécissements syphilitiques du rectum, Arch. gén. de méd., Paris **2**:666, 1854; cited by Hartmann.[10]

Jeffries, who was Tuttle's pathologist, described at the same time the French pathologists did that there was a destruction of the cylindric epithelial layer and that this was replaced by striated pavement epithelium.

Diffuse sclerosis of the submucosa, with amalgamation of all the coats of the bowel, decreased the number of blood vessels, but there were no changes in the arterial walls. The normal elements of the anal wall and the perineum and the fibers of the levator ani become thin or thinned out and lose their origin, and degeneration is manifest. Hartmann pointed out that a sclerolipomatous change takes place in the perirectal tissues and that the inflammation may spread to the pelvic part of the peritoneum, giving rise to adhesions in the pouch of Douglas.

A rectal biopsy specimen shows inflammatory tissue with many epithelioid cells in palisade formation, much increase in collagen fibrils and ofttimes giant cells and eosinophils. The palisade formation of the epithelioid cells may simulate a tubercle.

The pathologic changes of the disease, aside from the gross evidence of stricture of the rectum, consist, in its early stages, of a reddened friable mucosa which bleeds easily on touch or proctoscopic examination and which is due to thickening and ulceration. The thickening involves all layers of the rectal wall—the mucosa, submucosa and tunica. Ofttimes the three layers are fused into a hard and thickened, dense mass, in which the normal histology of the rectum is lost. The scar tissue extends deeply into the adjacent perirectal tissues, and if fistulous formation is present the scar tissue extends along the tract or tracts to the external surface of the body.

All fistulas are distal to the stricture. Proximal to the stricture there is ulceration and dilatation of the rectum or sigmoid in proportion to the degree of stenosis, with a superimposed, mixed secondary infection. The obstruction to the fecal outflow plus the secondary infection is the cause of many of the secondary symptoms presented by the patients, namely, low grade fever, constipation, anemia, weakness, dehydration and malnutrition.

Hartmann reported 15 cases in which the stricture involved the entire rectum. Sometimes the area above the stricture produces a red wine color and at other times a reddish yellow. This is due to superimposed secondary infection. In the anus the papillae swell, the derma becomes infiltrated and edematous skin tags, anal fissures, sinuses, fistulas and perianal granuloma occur.

Gypstein [35] was the first to note that a stricture of the rectum is uniform throughout its entire length and that there are no bands or valves present.

35. Gypstein, F.: Des effets d'électrolyse circulaire négative dans les rétrécissements fibreux du rectum, Thesis, Paris, no. 438, 1909-1910.

The rarer types of pathologic changes above the rectosigmoid are indicated in table 4. For example, Spiesman, Levy and Brotman reported a case which at autopsy showed lymphogranuloma venereum which involved the terminal part of the ileum and colon as well as the rectum.

An unusual but interesting case of fatal peritonitis from proctosalpingostomic fistula complicating a rectal stricture has been reported, with autopsy findings, by Pearce, Bower and Burns,[36] from the Philadephia General Hospital. A brief abstract of the necropsy is as follows:

> Bilateral, moderate hydrothorax and pleural adhesions of the left upper lobe were present. Both lungs were markedly edematous and a small embolus was evident in the right lower lobe. The heart demonstrated acute toxic degeneration. There was diffuse fibrino-purulent peritonitis. Right adnexae were absent. The spleen showed moderate pulpitis. The kidney and liver revealed acute toxic degeneration. The adrenals had lipoid depletion. The pelvic veins showed thrombosis. Old adhesions of the uterus and left adnexae were present. The rectum revealed advanced lymphogranuloma with a stricture two inches above the skin margin. Careful dissection demonstrated a fistula between the left side of the rectum, just above a stricture, and the left Fallopian tube near the ampulla. . . . The uterine end of the tube was occluded.

Rectal contents passed through the open end of the tube into the peritoneal cavity. This case proves conclusively that fistulas may occur above the site of stricture, although the usual site is below.

In all cases the degree of stenosis is in direct proportion to the amount of fibrosis and inflammatory reaction present.

Mathewson is the sole observer who was of the opinion that ulceration occurs only below the stricture, and this he admitted is difficult to explain, whereas Hartmann and others, including ourselves, have noted ulceration above the site of stricture. Mathewson assumed that the perirectal glands break down to form fistulas emptying into the rectum or perirectal tissue. He was also of the opinion that the inflammatory process seen in association with venereal lymphogranuloma does not subside after colostomy, as do infections which follow carcinoma or injuries to the bowel, while Woods and Hanlon stated that "colostomy has not been used with constant success in arresting the progress of the disease." The fact is that colostomy does cause the secondary infection to subside in some instances but is, in other instances, without effect on the progress of the virus infection, which explains the two views.

Responsible observers still differ as to the actual way in which the initial lesion in the rectal mucosa begins in women. From the evidence at hand, in women one cannot say whether the process begins primarily in the mucosa, as a result of lymphatic drainage from the site of virus

36. Pearce, A. E.; Bower, J. O., and Burns, J. C.: Fatal Peritonitis from Proctosalpingostomic Fistula Complicating Lymphopathia Venereum, Am. J. Surg. **69**:406 (Sept.) 1945.

entrance—although probably such is the case—and that the inflammation extends from the mucosa outward through the submucosa, muscularis and into the perirectal tissues or whether the process is a result of an extension from the perirectal tissues into the mucosa from without in. Some years ago one of us (L. T. W.) examined at autopsy the rectums of 18 women who had a positive Frei reaction, in the hope of adding light on this point, but none of these women showed any evidence of rectal involvement, and it was decided that this line of study was fruitless. It is our opinion, however, in the light of the frequency of proctitis without stricture of the rectum, that the virus in women is carried via the lymph channels directly to the mucosa and submucosa

TABLE 3.—*Classifications of Rectal Strictures by Different Authors*

Grace *	Peyton †	Sénèque ‡	Bensaude and Lambling [16]	Bacon §	Spiesman, Levy and Brotman #
1. Stricture with proctitis	1. Anal stricture	1. Pure stricture limited to rectum	1. Rectal stricture associated with an inguinal bubo	1. Stricture (alone)	1. Prestricture stage
2. Stricture without proctitis	2. Rectal annular (also linear) stricture	2. Rectal stricture with elephantiasis of external part	2. Rectal stricture associated with edema of the labia majora	2. Stricture and esthiomene	2. Rectal stricture (uncomplicated)
3. Proctitis without stricture	3. Rectal tubular stricture	3. Rectal stricture complicated with fistulas	3. Rectal stricture associated with inguinal bubo and edema of the labia majora	3. Esthiomene (alone)	3. Rectal stricture with anal growths or anal tags (cockscomb growths)
	4. Rectal communicating stricture	4. Rectal stricture with pelvic cellulitis	4. Simple rectal stricture with the external manifestations in the genitalia or in the ganglions	4. Abscess and fistulas (multiple)	4. Rectal stricture with sinuses, fistulas or granulomas ("watering pots")
				5. Postanal infection	5. Rectal stricture with elephantiasis, anal growths, sinuses (esthiomene)
				6. Ulcerative proctocolitis	6. Rectal stricture with pelvic pathologic conditions
				7. Anal stenosis	7. Stricture of the entire colon
					8. Rectal stricture with associated complications

* Grace, A. W.: J. A. M. A. **122**: 74, 1943

† Peyton, T. R.: Am. J. Syph., Gonor. & Ven. Dis. **24**: 360, 1940.

‡ Sénèque, J.: Bull. et mém. Soc. nat. de chir. **59**: 1233, 1933; Presse méd. **42**: 376, 1934; cited by Cole, H. N.: J. A. M.A. **101**: 1069, 1933.

§ Bacon, H. E.: Am. J. Digest. Dis. & Nutrition **2**: 570, 1935.

Spiesman, M. G.; Levy, R. C., and Brotman, D. M.: Am. J. Digest. Dis. & Nutrition **3**: 931, 1937.

themselves at the same time it is carried to the perirectal glands and tissues. The factor or factors that cause it to develop in these locations require further study. In the few women who have been passive partners in coitus per anum and in male pederasts, the problem is clear, namely, that there is a direct deposition of the virus on the mucosal wall and the process extends from within outward. In spite of the opinion of many important students of this disease, we believe that sodomy is a negligible factor in the production of stricture in women. It is hoped that further pathologic studies will clear up this point.

In table 3 we have listed the classifications of rectal strictures by different authors for purposes of comparison. Each of the classifications is of value within certain limitations, but, as our knowledge of the disease has grown, we have found that they were inadequate for purposes of a complete clinical understanding of the disease. The classification shown in table 4 was devised by one of us (L. T. W.) as an aid to a better understanding of the clinical problems involved.

TABLE 4.—*Classification of Rectal Strictures*

- I. Prestenotic proctitis
- II. Strictures; types *: (1) soft, regular; (2) hard, irregular; (3) firm, regular; (4) scirrhous
  - A. Simple (pure or limited); may be grades 1, 2, 3, 4 or 5 †
    - 1. Anal
    - 2. Rectal
      - (a) Annular (diaphragmatic)
        - (1) Single
          - (a) Lower rectum
          - (b) Midrectum
          - (c) Rectosigmoid
        - (2) Multiple
      - (b) Tubular
        - (1) Limited to a portion of rectum
        - (2) Massive (diffuse) (entire rectum)
    - 3. Colorectal
      - (a) Rectosigmoid
      - (b) Sigmoid (pure or alone)
      - (c) Rectum, sigmoid and descending colon
      - (d) Rectum and entire colon
    - 4. Ileorectal
      - (a) Rectum and ileum
  - B. Combined (with other pathologic conditions or "complications," with associated lesions and may involve any of organs as shown in simple strictures); may be grades 1, 2, 3, 4 or 5 † for rectum
    - 1. Local lymphogranulomatous lesions
      - (a) Bubo (inguinal adenitis)
      - (b) Anal tumors and papillomas
      - (c) Elephantiasis
      - (d) Fistulas
        - (1) rectal
        - (2) rectovaginal
        - (3) proctosalpingostomic
      - (e) Pelvic peritonitis—parametritis
      - (f) Diverticulosis
      - (g) Megacolon
      - (h) Osteomyelitis
      - (i) Urethral stricture (male and female
    - 2. Carcinoma of: (Usually anal; often superimposed on lymphogranuloma venereum)
      - (a) Anus
      - (b) Rectum
      - (c) Vulva
      - (d) Abdominal wall
    - 3. Infections (local and general)
      - (a) Syphilis
      - (b) Gonorrhea
      - (c) Chancroids
      - (d) Tuberculosis

* Type 1 is soft, smooth and regular due to mucosal edema and congestion; type 2 is hard and irregular, with granulomatous deposits in the mucosa and submucosa; type 3 is small amount of scar tissue in the submucosa and muscularis, and type 4 is dense scar tissue in all layers of the rectum and perirectal tissues.

† Measurement by means of bougies or rectal dilators; grade 1 admits 1½ inch (3.7 cm.); grade 2 admits 1 inch (2.5 cm.); grade 3 admits ½ inch (1.2 cm.); grade 4 admits ¾ inch (0.6 cm.), and grade 5 admits none.

Marino [37] used the proctoscope as a means of measuring stricture lumens. The diagnosis in cases of pure uncomplicated strictures of the rectum is made by means of the examining finger. External manifestations of the disease in all cases demand a rectal examination.

37. Marino, A. W. M.; Buda, A. M.; Turell, R., and Nerb, L.: The Treatment of Venereal Lymphogranuloma with Sulfanilamide, Am. J. Surg. **46**:343 (Nov.) 1939. Marino, A. W. M.: The Anorectal Aspect of Venereal Lymphogranuloma, ibid. **45**:293 (Aug.) 1939.

Obvious stigmas of strictures of the rectum make the diagnosis easy if the patient presents elephantiasis of the vulva (figs. 4 and 5), anal tags (fig. 1), fistulas, fissures, cockscomb tumors (fig. 2) or papillomatous tumors around the anus which are obviously of a benign nature. The

Fig. 1 (patient S. A.).—Anal edema with tags. Stricture of the rectum of six years' duration.

Fig. 2 (patient M. B.).—Artist's drawing of cockscomb growth, showing anal tumor, stricture of the rectum and fibroid of the uterus. A photograph of this tumor was published by us in a previous paper.[1e]

reason for this is that practically all physicians today make a rectal examination in such cases. Incidentally, these tumors may grow to

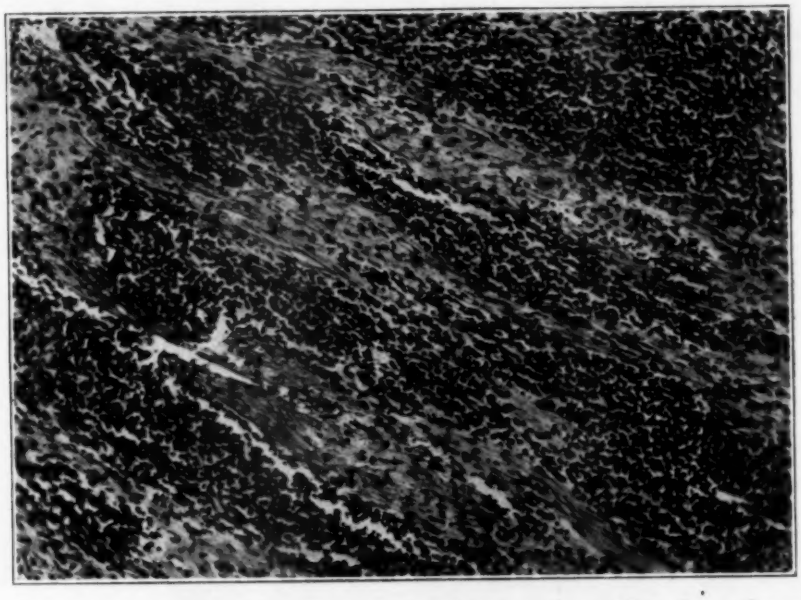

Fig. 3 (patient M. B.).—Photomicrograph of sections taken from the anal tumor, showing bands of lymphocytic infiltration among bands of fibrous tissue.

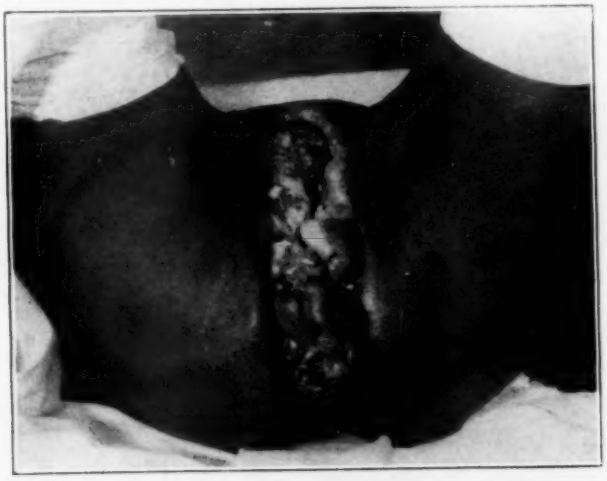

Fig. 4 (patient T. S.).—Multiple tumors involving the labia majora and minora, perineum and anus, with stricture of the rectum. The condition began eighteen years before this article was written. Edema is slight or absent.

the size of one's fist. Cryptitis is often present. Fistulas with a growth of granulation tissue around the fistulous opening or openings are not uncommon. At times there is a simple rectovaginal fistula, but we

have seen cases in which the rectovaginal septum has been almost completely eroded or destroyed near the anus and also involved the perineal muscles.

In a few cases there is a phagedenic ulcer that extends from the anus into the vagina, destroying the perineal body; sometimes these ulcers have hard edges. Often in such cases there is a superimposed anal carcinoma or cancer occurring in association with the lymphogranulomatous condition. Liccione [38] was the first to point out the coexistence

Fig. 5 (patient S. D.).—Elephantiasis of the vulva and clitoris, with massive tumor of the right labia minora with stricture of the rectum. The tumor was extirpated, and abdominoperineal resection of the stricture was done. Squamous cell carcinoma of the left edge of the vagina and rectum developed. The carcinoma was treated with radium. Several weeks later there developed numerous sinuses discharging pus from an ulcer of the left side of the vagina and upper part of the left leg. The patient died; autopsy was not done. The photograph was secured through the courtesy of Dr. M. E. Ross, with whom the senior author saw the patient in consultation. The case was described in detail in a previous article by us.[10]

38. Liccione, W. T.: Venereal Stricture of Rectum: Adenocarcinoma as a Late Complication of Lymphogranuloma Inguinale, Am. J. Surg. **31**:551 (March) 1936.

of carcinoma and rectal strictures. Carcinoma of the rectum sometimes produces a stricture which simulates stricture due to lymphogranuloma venereum.

In 27 cases in this series the diagnosis of rectal stricture was first made in our obstetric service after the patient was admitted to the hospital in labor by the obstetrician who made a rectal examination on these patients. They were patients who had failed to visit the prenatal clinic.

In most cases rectal examination shows the rectal wall to be thickened and narrowed. The lumen may admit the tip of the index finger, or there may be almost complete occlusion, which will barely permit the passage of a ureteral catheter.

The diagnosis may be confirmed by proctoscopic examination if an anal stricture does not preclude the use of a proctoscope.

Our records show that the Frei test was performed many times in cases in which, unfortunately, they were not recorded. Of 118 cases, it was positive in 91, or 77.1 per cent, and negative in 27, or 22.9 per cent. In some instances the original Frei antigen was used, in some the mouse brain antigen was used and at present we are using the chick embryo antigen.[39] Although an important adjunct in the diagnosis of the disease, the Frei test is not absolutely specific and negative reactions occur in a sufficient number of cases for us not to place the absolute reliance on the test that we would have a few years ago. Some negative reactions to the Frei test were undoubtedly due to faulty technic in the performance of the test, because in many instances positive reactions have been obtained when a retest was insisted on. It should, however, be done in all cases of suspected strictures, and when positive it is a most important confirmatory diagnostic aid. If negative, it is important to repeat the test with potent antigen and scrupulously careful technic. The cultivation of the virus from the rectal mucosa obtained from the site of the stricture, of course, makes the diagnosis absolute.

Hyperproteinemia with a definite increase in serum globulins in excess of 3.5 per cent in lymphogranuloma venereum was first noted by Gutman.[40] It is a suggestive diagnostic sign that has been confirmed by us. The reversal of the albumin-globulin ratio in early and late cases, which persists as long as any active infection remains, is stressed by Howard, Eisenman and Strauss.[41] We have found it to be present in all cases, with the condition active or otherwise, during the past six

39. Lygranum, as kindly supplied us by E. R. Squibb & Sons.

40. Gutman, A. B.: Systemic Manifestations of Lymphogranuloma Venereum, New York State J. Med. **39**:1420 (July 15) 1939.

41. Howard, M. E.; Eisenman, A. J., and Strauss, M. J.: Alterations in the Serum Proteins in Lymphopathia Venerea, Am. J. Syph., Gonor. & Ven. Dis. **23**:83 (Jan.) 1939.

months. Gutman considered hyperproteinemia as a reflection of the immune response of the organism to the infection. The sedimentation rate has not been a diagnostic help in these cases.

The anemia and amyloid changes are those found in all chronic diseases and are not specific.

Biopsy should be used in two ways: (1) to rule out the presence of a coexisting carcinoma as a result of histologic study, although the presence of carcinoma should not prevent one from attempting to isolate the virus, because carcinoma is often superimposed on lymphogranuloma, and (2) to isolate the virus in institutions where laboratory facilities make this procedure possible, and it is our opinion that it will be increasingly used. In this series of cases biopsies were done in 34 instances, but virus isolation studies were not done, although at the present time we are undertaking this method of study.

TABLE 5.—*First Symptom in 461 Cases*

First Symptom	Cases, No.
Constipation	172
Rectal bleeding	49
Alternating constipation and diarrhea	40
Ribbon stools (narrowed, thin or pencil-like)	39
Anal fistulas	36
Abdominal pain (without other obstructive symptoms)	24
Colostomies	24
Purulent discharge	23
Acute intestinal obstruction (pain and vomiting)	23
Pain on defecation	12
Diarrhea	11
Pruritus ani	4
Abdominal catastrophe (rupture of rectum following dilatation in clinic)	4
Total	461

The Wassermann test was carried out and recorded in 287 cases, the reactions in 91, or 31.4 per cent, being positive and in 196, or 68.6 per cent, negative. At the present time the Frei test is routinely done on all patients in our proctology clinic, as is a Wassermann test. In some instances we do a complement fixation test for lymphogranuloma, although the patient may not have any suggestive symptoms of the disease.

In table 5 we have listed the leading symptoms in 461 cases. From that table it is seen that constipation, rectal bleeding, alternating constipation and diarrhea and ribbon stools occur most frequently. In 5 patients in this series the diagnosis was made of ulcerative colitis.

In table 6 we have recorded the lesions combined with strictures of the rectum.

The location of the stricture was definite in 182 cases, as shown in table 7, which is a fairly representative average percentage for the entire series.

The signs and symptoms obviously vary according to the location and degree of the stricture. (See figs. 6, 7 *A*, 8 and 9.)

Some patients have come to the hospital with pneumonia, and the stricture of the rectum was an incidental finding. Fibroids are frequently found in association with lymphogranuloma. Tuberculosis is a frequent concomitant infection in this disease. Many of the patients come into the hospital during an acute episode, with either abdominal pain, vomiting, pain in the rectum or constipation, and, as soon as the acute episode has passed, in one or two days, they leave the hospital without permission; this necessarily makes the hospital records incomplete, because the patients do not remain sufficiently long to be properly studied.

TABLE 6.—*Lymphogranulomatous Lesions Associated with Rectal Strictures*

Lesion	Cases, No.
Anal fistulas	58
Rectovaginal fistulas	34
Perianal tags or cockscomb growths	22
Hemorrhoids	17
Elephantiasis of the vulva (esthiomene)	11
Carcinoma	6
Arthrtis	4
Osteomyelitis	4
Pelvic peritonitis	3
Elephantiasis of penis or scrotum and stricture of urethra	1
Ovarian tumor (pathologic examination showed to be lymphogranuloma)	1
Total	161

It has been hard for the patients to determine the exact time of onset of the stricture. One third of the patients stated that it had been of one year's duration, another third stated that it had been of two years' duration and in the remainder of our cases it varied up to twenty-two years or more.

TABLE 7.—*Location of the Stricture*

Location	Cases, No.
Lower part of the rectum involved	138
Entire rectum involved	30
Sigmoid involved	8
More than one stricture, different levels	6
Total	182

Seventy-seven women in this group of cases had children before they were aware of the fact that they had a stricture, and 22 women in this series have borne children after the diagnosis of stricture was made. It is clear, therefore, that lymphogranuloma per se does not preclude the possibility of pregnancy, although there is some evidence that infected women are not so fertile as those without the infection.

Kassebohn and Schreiber were the first to report rupture of the rectum caused by rectal stricture during childbirth. Subsequently, they reported 18 cases of rectal stricture at childbirth at full term from the

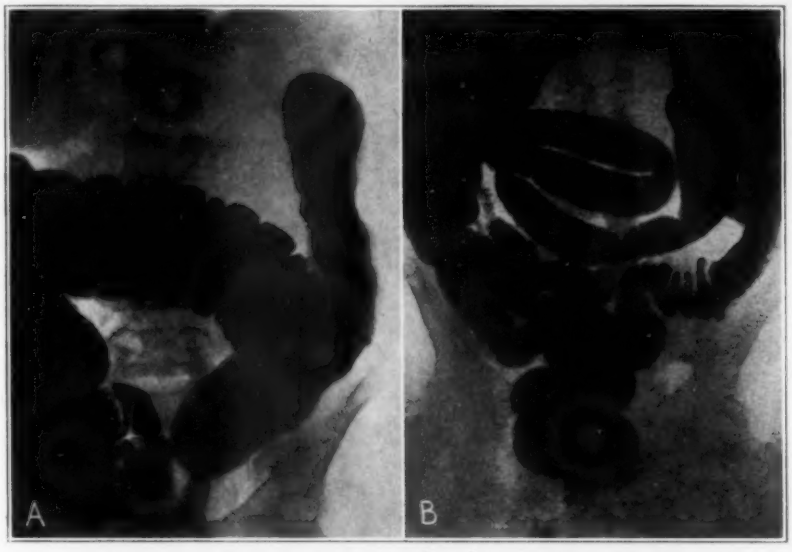

Fig. 6.—*A*, roentgenogram of barium enema in patient L. J. There was a stricture of the rectum 2 inches (5 cm.) from the anus. *B*, roentgenogram of barium enema in patient R. E. The stricture of the anus was of five years' duration. No previous operation was performed.

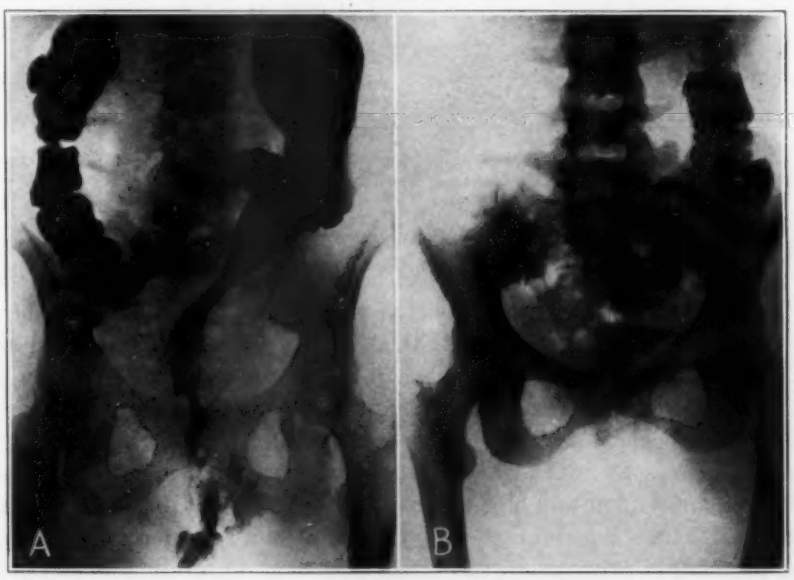

Fig. 7.—*A*, roentgenogram of barium enema in patient F. J. A stricture of the rectum and sigmoid with multiple anal fistulas was present. *B*, roentgenogram of rectal stricture with numerous draining sinuses in patient A. T.

obstetric service at Harlem Hospital. They advised therapeutic abortion if the presence is discovered early, and in cases in which this is impractical (the religious viewpoint may enter) pregnancy may be permitted to proceed, with an attempt at spontaneous delivery or cesarean section, but in no circumstances should instrumental delivery be attempted.

Fig. 8 (patient E. H.).—Roentgenogram of barium enema. There was a stricture involving the entire rectum, with a fistula in ano.

LABORATORY FINDINGS

The most constant finding has been low grade secondary anemia. The red cell count has averaged between 3,500,000 and 4,000,000. Many patients showing a count of 4,000,000 cells were so dehydrated that hemoconcentration had to be taken into consideration. The white cell count showed no special change except during crises of one type or another. Urinary findings have been, on the whole, normal. One patient in this series had diabetes. Urea nitrogen and creatine levels, blood sugar content and blood chloride levels were, on the whole, usually normal. The sedimentation rate, on the whole, was normal, except in the presence of pronounced secondary infection. Determinations of blood fibrinogen were made in about 30 of these cases, and they were within normal range.

ROENTGENOGRAPHIC EXAMINATION

Barium enemas have been used in over 100 of these cases, and they demonstrated the presence of stricture. It is invaluable in cases of high stricture (fig. 11 *A*) because only through its use can information be obtained as to the underlying pathologic changes. One disadvantage of the barium enema is that in narrow strictures the barium may become inspissated and thus at times aggravate the clinical condition of an extremely sick patient. In low strictures, we have used, with success, a balloon passed through the stricture, and it is then filled with sodium iodide and the roentgenogram taken (fig. 9). This has given us accurate information as to the length of the stricture, without any of the disadvantages from inspissation of the barium when used as an enema. In acute intestinal obstruction superimposed on the chronic obstruction

Fig. 9 (patient C. J.).—Roentgenogram of a rubber balloon introduced through the stricture and filled with sodium iodide solution. This shows the stricture of the lower one half of the rectum. It indicates the ease with which, in selected cases, this technic is used and that it is preferable to that of a barium enema. There is no inspissation of the barium above the site of the stricture.

that is present in these cases, flat roentgenograms show distention of the large bowel and, in some instances, distention of the small intestines, with fluid levels.

DIAGNOSIS

The diagnosis is relatively simple if the stricture is located low in the rectum. The chief point to remember is that a rectal examination should be made in any patient presenting symptoms of constipation, deformed or ribbon-like stools, hemorrhage per rectum or a discharge of pus per rectum. Elephantiasis of the vulva or scrotum or anal tags are only additional clues which indicate that a rectal examination should be made. Proctoscopic examination is sometimes valuable in confirming

the diagnosis. Proctoscopy and sigmoidoscopy are helpful if the lesion is in the rectum or rectosigmoid areas. Care must be used in making a proctoscopic examination, because of the danger of rupture of a diseased rectal wall. The Frei test, the complement fixation test and the albumin-globulin ratio are valuable diagnostic aids. Roentgenologic examination is important in strictures that are above the reach of the finger or the proctoscope. Biopsy will prove the presence of granulomatous tissue, and, of course, the isolation of the virus makes the diagnosis absolute.

DIFFERENTIAL DIAGNOSIS

1. Intestinal tuberculosis may cause formation of strictures as a part of tuberculosis of the intestinal tract.

2. In ulcerative colitis the diarrhea, dehydration, loss of weight and anemia may cause one to consider lymphogranuloma venereum as the causative agent.

3. Carcinoma of the rectum without lymphogranuloma has to be ruled out. Liccione, however, described 2 cases of adenocarcinoma of the rectum superimposed on lymphogranuloma. Woods and Hanlon and Barber and Murphy [42] have each described 3 cases in their series. We have found carcinoma superimposed on lymphogranuloma in 5 instances.

4. Diverticulitis may produce any of the symptoms caused by lymphogranuloma venereum, such as diarrhea, constipation and rectal bleeding. Roentgenographic examination by means of a barium enema makes the diagnosis clear. Chronic diverticulitis can result from rectal stricture, as shown in the case of Phemister's cited by David and Lauer.[43]

5. Chemical strictures must be ruled out. Rosser described a chemical stricture of the rectum, which is relatively rare. The patients give a history of receiving injection treatments for hemorrhoids.

Strictures due to parasites, amebic ulcers and other conditions are so rare in this country that they need only to be mentioned.

PROGNOSIS

Rectal strictures due to lymphogranuloma venereum are the most serious clinical condition that results, on a large scale, from this disease. Many persons in whom strictures of the rectum develop live to a relatively extreme old age. In other instances, the stenosis of the rectum not only causes disability and prolonged morbidity, but it is

42. Barber, W. H., and Murphy, W. B.: Lymphogranuloma Venereum, Ann. Surg. **113**:30 (Jan.) 1941.

43. David, V. C., and Lauer, C. A.: Stricture of the Rectum with a Consideration of Some Unusual Causes, J. A. M. A. **98**:1 (Jan. 2) 1932.

the real cause of death in many instances. The disease is progressive at times, oftener it is apparently static and in the present state of our knowledge it is impossible for any one to isolate with accuracy the conditions that will progress from those that will not, due to many not fully understood factors. Worth while mortality statistics cannot be produced, because of this fact and also because the patients roam from doctor to doctor and from clinic to clinic.

Tuberculosis develops as a death-producing factor in a large number of these cases. Pneumonia here in New York is a serious factor in other instances. Acute and chronic intestinal obstruction develops not infrequently. It has been stated that strictures of the rectum never cause death but are always present at the time of death. Rectal strictures are a common cause of death, but often the death-producing factor is not considered to be the stricture, because of other complications.

TREATMENT

Numerous methods of treatment have been used in these cases. The scope of this paper permits only a brief discussion of a few of them.

Drugs.—For many years fuadin was used in our clinic, without success. Shropshear [44] was the first to use sulfanilamide in these cases. Grace recommended sulfathiazole. Levy, Holder and Bullowa treated 120 patients in our clinic with sodium sulfanilyl sulfanilate and were impressed by the immediate results obtained. Subsequent follow-up after three years has been unimpressive. This is not taken to mean that the use of sulfonamide drugs in the prestricture stage of the disease may not in some instances prevent further progress of the condition and in this way stop formation of strictures. The cases in which this may occur we cannot state with certainty. We are sure, however, that sulfathiazole, sulfanilyl sulfanilate and succinylsulfathiazole will clear up much of the secondary superimposed infection and in this indirect way improve the condition of the patient. No evidence has been forthcoming that sulfonamide drugs are viricidal in their action. At present we are using phthalylsulfathiazole. Antimony and potassium tartrate, as recommended and used by Stone,[45] has proved valueless except as a mild general tonic. We have used penicillin in a few cases recently, and this has proved less successful than the sulfonamide compounds. Certain conditions will go on to serious formation of fibrous strictures

44. Shropshear, G.: Sulfanilamide in the Treatment of Strictures of the Rectum Caused by Lymphogranuloma Venereum, Illinois M. J. **74**:153 (Aug.) 1938.

45. Stone, H. B.: Stricture of the Rectum; Carcinoma of the Rectum, J. South. Med. & Surg. **98**:1 (Jan.) 1936.

in spite of drugs in cases in which the virus shows real pathogenic activity. In patients in whom the symptoms and signs are predominantly due to congestion, edema and ulceration caused by secondary infection, sulfonamide drugs are of positive value, but they cannot and do not cure fibrous stricture of the rectum, because of (1) lack of viricidal potency and (2) poor vascularity of scar tissue, which will not permit sufficient concentration of the drug at the point where it is needed to be of effective consequence. It is obvious that drugs cannot remove scar tissue.

Biologic Methods.—A. Antigens: Frei antigen has been used in our clinic and in many other clinics and is still recommended by some clinicians as a method of treatment. In our clinic at least it has proved to be valueless. It has been used in over 200 cases, without effect. Seidenstein [46] used Frei antigen with sulfonamide drugs. Frei himself stated that the use of Frei antigen or the cutaneous test may produce an acute exacerbation of a local lesion. This we have never observed.

B. Estrogens: Seley, Vernick and Goldman [47] reported improvement in 4 patients treated with parahydroxyphenyl ethyl hexane, a dose of 30 mg. a day being used. The basis for the use of estrogens, as explained by them, is that pregnancy seemed to help rectal strictures by causing a softening of the genital, pelvic and perineal tissues during childbirth. Palmer, Kirsner and Rodaniche reported that pregnancy seemed to help their patients. Schreiber [48] denied this, and in support he quoted the statistics of our obstetric department.

C. Irradiation: We have had no experience with the use of deep roentgen therapy or of radium in these conditions, and for that reason we are unable to make a definite statement. We have had a few patients come to us having advanced strictures who had received radium therapy in other institutions. It did not seem to us that the pathologic changes or the progress of the condition had been lessened, because when we saw these patients their lesions had continued to advance in spite of their radiation therapy.

D. Diathermy: The literature is replete with reports of cases in which diathermy has softened the stricture and in some cases caused a retrogression of the stricture. Years ago, diathermy was used in the clinic of this hospital, and its results were totally unsatisfactory.

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46. Seidenstein, H. R.: Rectal Stricture Due to Lymphogranuloma Venereum: Treatment with a Sulfonamide and Frei Antigen, Surgery **14**:73 (July) 1943.

47. Seley, A. D.; Vernick, S., and Goldman, H.: The Estrogen Treatment of Stricture of the Rectum Due to Lymphogranuloma Venereum, J. Clin. Endocrinol. **5**:301 (Sept.) 1945.

48. Schreiber, M. J.: Personal communication to the authors.

E. Solid Carbon Dioxide.—Solid carbon dioxide was used, ineffectually, in a large number of cases in our outpatient department over a period of several years, and it was discarded because it served no useful purpose.

Surgical Methods.—A. Dilation: Dilation by finger and bougies has been widely used. Finger dilation is a safe method in conditions that are not too far advanced. It cannot be used in strictures beyond grade 3. Dilation of these strictures by means of bougies has resulted in death at times, as evidenced by the report of Woods and Hanlon of seven deaths in 192 cases. In our clinic four deaths occurred. In 1 case early operation prevented death, and in this case colostomy in the transverse colon was performed and also drainage of the abdomen after the rent in the rectum had been sutured. The use of Wales bougies and other mechanical methods of instrumental dilation has been surgery's chief weapon in its attack on this condition. The only objection to the use of bougies and other mechanical dilators is that they tear the stricture, and this increased trauma stimulates greatly the subsequent formation of scar tissue; in fact, the late condition of many of these patients is worse owing to the extra scar tissue caused by the dilation. In certain selected cases dilation is a valuable palliative method of treatment to be used with judgment by surgeons who have a thorough understanding of the pathologic changes.

B. Internal Proctotomy: Internal proctotomy, which means to divide the stricture within the rectum by means of an incision, is similar in every way to the operation of internal urethrotomy. Surgeons who advise its use maintain that the ultimate results depend on the care with which the stricture is kept dilated. We have used it in selected cases, although we were aware at the time of the fact that it was not a satisfactory definitive method of treatment, because the trauma produced by this procedure stimulated the production of more scar tissue, which after a few months made the stricture much more rigid and sometimes impassable. Internal proctotomy, in our opinion, is only a palliative method of treatment for stricture at the time when fistulas are being excised and as a part of a plan of treatment preliminary to colostomy in greatly weakened patients. This, of course, varies with the individual case, because we feel that it is better to do an internal proctotomy and give the patient temporary relief as a preliminary to other planned procedures. Most surgeons agree that internal proctotomy is not a sound method of treatment per se.

C. Complete or External Proctotomy: Complete or external proctotomy means an incision through the stricture and the posterior

commissure extending down to the tip of the coccyx, which includes throughout its entirety the anal sphincter posteriorly. Bougies have to be used after the operation. Hartmann reported that he performed sixteen such operations in 1895, and the results were unsatisfactory. This operation, as experienced in a number of cases, not only adds to the amount of scar tissue already present but greatly stimulates the subsequent cicatrix so that it is more pronounced than before. We used this operation in a number of cases some years ago, and we agree with Hartmann that it is not a curative procedure but only palliative and that the only justification for its use is a part of a plan in which subsequent corrective procedures are contemplated.

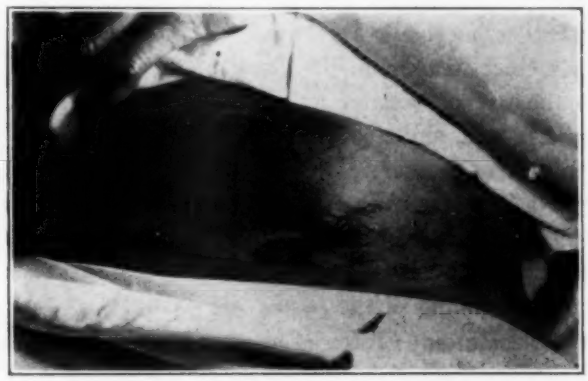

Fig. 10 (patient B. T.).—Sponantous closure of colostomy for rectal stricture. Six months after colostomy, bowel movements per rectum became normal. This shows the appearance of the colostomy six years later. Occasionally a bit of flatus passes through the colostomy. This illustrates the beneficial effects of colostomy alone in certain cases. The patient has had a course of treatment with sulfonamide drugs since the colostomy.

D. Permanent Colostomy: Permanent colostomy is the operative procedure of choice of most American surgeons. Tuttle and other earlier surgeons, as well as Mathewson, Woods and Hanlon and others, agreed that it does not stop the progress of the disease. In most instances, the patients are relieved of pain, they gain in weight and their clinical condition improves considerably. The disadvantages are (1) objection by the patient to a permanent artificial anus, (2) stricture of the colostomy opening and at times infection around the stoma, (3) anterior grade herniation of the bowel through the colostomy opening and (4) retrograde herniation through the bowel through the colostomy opening (figs. 10, 12, 13 and 14). In some instances permanent colostomy, in which the stricture is not resectable, is the

only operation possible for the surgeon to perform, and in these cases it is life saving. A permanent colostomy is necessary in all cases in which an abdominoperineal resection of the rectum is indicated. A more detailed discussion of colostomy for rectal strictures was presented by us in a previous paper.[1e]

Fig. 11 (patient V. M.).—*A*, stricture of the sigmoid and rectum. *B*, mottling of the third and fourth lumbar vertebrae, indicating osseous involvement.

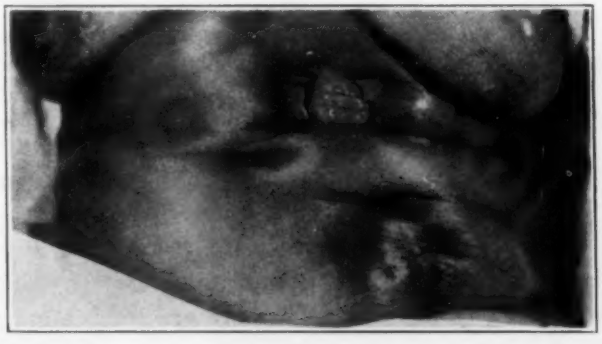

Fig. 12 (patient C. B.).—The patient, aged 60, had a rectal stricture for forty years. Left inguinal colostomy was done twenty-four years after it appeared and double-barreled colostomy one year later because the left inguinal colostomy became strictured. The second colostomy continues to function well, but discharge from the left inguinal colostomy began after fifteen years. This subsided, and the lesion healed after three weeks' treatment with phthalylsulfathiazole.

E. Warthen's [49] Operation. Warthen's operation is a modified permanent colostomy operation devised for patients with rectal strictures. He obliterates the cul-de-sac of Douglas by painting it with one-half strength tincture of iodine solution and then uses a series of purse string sutures of chromic surgical gut in each fossa lateral to the rectum. A double-barreled colostomy is then performed through a McBurney incision on the left. Warthen treated 10 patients in this way. The only possible advantage of Warthen's operation—and this is still to be proved—is that it may prevent anterior grade or retrograde herniation.

F. Temporary Colostomy: The chief indication for the performance of a temporary colostomy occurs in cases in which it is planned to do a resection of the rectum with preservation of the anal sphincter.

Fig. 13 (patient L. H.).—The patient had a right inguinal bubo twenty-one years before we saw her. There was a history of rectal stricture for sixteen years, foul rectal discharge with odor and rectal hemorrhages for eleven years and colostomy was done three years before this article was written because of vomiting and abdominal distention. There is massive herniation of the abdominal wall at the site of the colostomy. Scars of previous buboes are to be noted.

G. Jelk's [50] Operation: The operation consists of bilateral incisions up to and beyond the upper border of the stricture. The stricture is divided by turning the knife blade toward the intestinal wall, with the finger in the rectum as a guide. The mucosa is left intact. The ulcerated mucosa is treated with antiseptics. The lateral incisions are drained with

49. Warthen, H. J.: Operative Treatment for Benign Rectal Stricture (Lymphogranuloma Venereum): Preliminary Report, Arch. Surg. **38**:617 (April) 1939.

50. Jelk, J. L.: A New Operation for Rectal Stricture, Tr. Am. Proct. Soc. **32**:19, 1931.

iodoform gauze. Bacon, Murray and Schoenfeld [51] operated on 24 patients, and these patients were symptomatically improved. We carried out this procedure in several cases, and the results were unsatisfactory.

H. Lockhart-Mummery and Lloyd-Davies [52] Operation: The coccyx is removed, the postrectal fascia is divided and the rectum is drawn into the wound, which permits a longitudinal incision of the stricture. The incision is sutured transversely. In the 2 patients that we have seen on whom this operation was performed, the results were failures.

Fig. 14 (patient A. W.).—Anterior grade and posterior grade prolapse of the colostomy in the transverse colon. Left inguinal colostomy had been performed in another hospital eleven years before the patient's admission to the hospital. Right inguinal colostomy had been performed ten years later. The left inguinal colostomy is completely healed. The right rectus colostomy shows a serious degree of prolapse. With phthalylsulfathiazole as preoperative medication, the prolapsed segments of the transverse colon were resected and the patient was discharged, improved.

I. The Stone Operation: Harvey Stone divides longitudinally the posterior vaginal and anterior rectal walls, suturing the edges of the vaginal incision to the edges of the rectal mucosa. A flap on each side of the vaginal mucosa is dissected up and sutured to the midline. The free edges of the vaginal mucosa are brought together over these free

51. Bacon, H. E.; Murray, F. H., and Schoenfeld, J. D.: Rationale of Jelk's Operation for Rectal Stricture: Preliminary Report, Am. J. Surg. **27**:476 (March) 1935.

52. Lockhart-Mummery, J. P., and Lloyd-Davies, O. V.: The Operative Treatment of Fibrous Stricture of the Rectum with the Description of a New Technique, Brit. J. Surg. **23**:19 (July) 1935.

flaps, thereby grafting normal vaginal mucosa into the stricture in order to establish a lumen. Lockhart-Mummery objected to this operation because of the danger of forming rectovaginal fistulas. We have had no experience with this procedure.

J. Keller's [53] Tunnel Skin Graft Operation: In 1933, Keller advocated the use of tunnel skin grafts in the treatment of strictures of the rectum. Full thickness grafts are taken from a hair-free area. A trocar and cannula are passed under the stricture. The trocar is withdrawn, a cannula being left in place under the mucous membrane. The graft is attached to a black silk ligature by means of a carrier. The graft is drawn into position by the exertion of a pull on the ligature pulled through the stricture. Usually three or four grafts are placed at equal distant points. Pressure is maintained with a distended Hagner or Pilcher bag. The bowels are not allowed to move for seven days. Keller reported on 8 cases. We have found this operation to be of value only in cases of anal stricture. Most anal strictures are due to a previous operation and are not due to lymphogranuloma. In extremely low lymphogranulomatous strictures it may be of value.

K. Hartmann's Sacroperineal Operation: Hartmann reported satisfactory results with a sacroperineal operation and preservation of the sphincter in a large number of cases. Although we have had no experience with Hartmann's operative procedure, we are of the opinion, because of his great knowledge of the disease, that it is worthy of extensive investigation and trial.

L. Pauchet's [54] Intrasphincteric Excision Operation: This operation, which we have used in 26 cases, is an endoanal excision of the rectum, with preservation of the sphincter following, in most cases, a temporary colostomy, the healthy rectum later being brought down through the sphincter and sutured to the skin. In 2 cases we have performed this operation in one stage, but in these 2 cases the pouch of Douglas was not opened. In our hands, Pauchet's operation has proved to be a worth while and satisfactory operation, which we can recommend wholeheartedly. The operation, however, can be used only in selected cases. If the stricture extends for more than 6 inches (15 cm.) above the anus, the procedure cannot be used. It also cannot be used if the sigmoid is plastered down with adhesions within the abdominal cavity. It should be used only by experienced surgeons and then in carefully selected cases.

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53. Keller, W. L.: Annular Stricture of the Rectum and Anus: Treatment by Tunnel Skin Graft; Preliminary Report, Am. J. Surg. **20**:28 (April) 1933.

54. Pauchet, V.: Practical Surgery Illustrated, London, Ernest Benn, Ltd., 1925, vol. 4, p. 195.

M. Abdominoperineal Resection Operation: Edwards and Kindell,[55] Barber and Murphy and Woods and Hanlon have reported excellent results from abdominoperineal extirpation of the diseased rectum and the formation of a permanent colostomy. In our opinion the indication for an operation utilizing the abdominoperineal excision is the fact that the strictured area involves the entire rectum or rectosigmoid; because of the extent of the disease it is impossible to bring down the proximal loop of bowel to the anus after the diseased area has been excised. We would add, as an additional prerequisite for such an extensive operation, that the patient should show clinical signs of disease activity of a serious nature which do not subside after a permanent colostomy.

ABSTRACTS OF HISTORIES IN CERTAIN ILLUSTRATIVE CASES

CASE 1.—*Simple stricture of the rectum; pronounced constipation.*

The patient was a Negro woman 30 years of age. There had been severe constipation, which during the past year had become progressively worse. Stools came out in thin strips and at times were streaked on the outside with bright red blood. During the past year the patient had lost 20 pounds (9.1 Kg.) in weight and had complained of vaginal discharge with itching. A rectal stricture was found 1½ inches (3.8 cm.) above the anal opening, which admitted the tip of the finger. Reaction to the Frei test was positive, and the Kahn reaction of the blood was negative.

CASE 2.—*Stricture of the rectum with diarrhea.*

A Negro woman 33 years of age entered the hospital with a temperature of 100 F. She had had a tooth extracted twenty days before. Eleven days before admission there developed diarrhea of five loose, watery stools per day. There was tenderness in both fornices on vaginal examination. Rectal examination revealed an annular stricture that was tender and indurated and which admitted the tip of the index finger. Proctoscopic examination revealed ulceration above the site of the stricture. With a regimen of rest and irrigations high in the colon the patient improved, and she left the hospital nine days later, without permission.

CASE 3.—*Stricture of the rectum with alternating constipation, diarrhea with blood and mucus in stools; colostomy.*

A Negro woman 45 years of age entered the hospital complaining of constipation alternating with diarrhea and with blood and mucus in the stools. She stated that she had lost a large amount of weight. The stools were ribbon-like in character. There were three or four perianal sinuses discharging pus about the anus. Digital examination of the rectum revealed a stricture 3 inches (7.6 cm.) above the anal orifice. Proctoscopic examination showed an area of induration and ulceration about the stricture and above the stricture. Reaction to the Frei test was positive. A biopsy specimen from the rectum showed acute inflammation. Left inguinal colostomy was performed ten days after admission. The patient was discharged three weeks later, improved.

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55. Edwards, M., and Kindell, F. B.: The Treatment of Rectal Lymphogranuloma by Excision, Surgery **4**:809 (Dec.) 1938.

CASE 4.—*Constipation and bleeding per rectum; colostomy.*

A Negro woman 33 years of age had had pain and bleeding per rectum on defecation for the past eighteen months. She had been treated in the clinic for some months. The reaction to the Frei test was positive. Digital examination of the rectum revealed a stricture which did not admit the tip of the index finger. Barium enema showed a stricture involving the rectum and sigmoid. At the time of the colostomy operation the roentgenologic findings were confirmed. The patient was discharged two weeks later, improved.

CASE 5.—*Double stricture of the rectum, rectal fistula, pencil-like stools and blood and pus from rectum on defecation.*

The patient was a white man 35 years of age. There was a history of ulcer of the penis followed by bubo eleven years before admission. During the past eight years he has suffered from constipation. Eight months ago he began to have pencil-like stools and passage of blood and pus from the rectum. Five months ago a rectal fistula developed. Barium enema showed a narrowing annular stricture of the rectum 5 cm. in length. With the patient under spinal anesthesia, one stricture was found 1½ inches (3.8 cm.) from the anus, and after this was dilated a second stricture was found 2½ inches (6 cm.) from the anus. These were dilated, and he was discharged, improved.

The foregoing cases are typical of the symptoms and physical findings noted in the majority of cases of rectal stenosis and are highly characteristic.

CASE 6.—*Stricture of the rectum with rectovaginal fistulas.*

The patient was a Negro woman 40 years of age who entered the hospital complaining of passage of stool through the vagina. Seven years ago she began to have many rectal abscesses, and four years ago she began to pass feces through her vagina. She had complained of mucous diarrhea and had lost some weight during the past year. Physical examination showed a fistulous opening into the vagina 1 inch (2.5 cm.) above the fourchet and a stricture of the rectum ½ inch (1.27 cm.) above the anal orifice, which barely admitted the tip of a finger. Reaction to the Frei test was strongly positive. The Kahn test elicited a negative reaction. While under a regimen of high colonic irrigations, the patient left the hospital one week later, without permission.

CASE 7.—*Stricture of the rectum, with ulcers of the vulva.*

The patient was a Negro woman 48 years of age. She had had three children, the last child now being 24 years of age. The chief complaint was pruritus vulvae, urinary incontinence and painful defecation. The patient had visited many clinics during the past six years, without relief, and the continuous dribbling of urine was particularly disturbing to her. On physical examination she showed the urethral meatus everted, and the external genitalia were deformed by a sloughing off of the posterior extremities of the labia. On separation of the labia, there were several areas of varying size where the mucosa was missing and the submucosal tissue presented. A tight stricture of the rectum was noted on digital examination of the rectum. The Kahn reaction of the blood was negative, and the urine was normal. The blood count showed 3,840,000 red cells, 60 per cent hemoglobin and 7,400 leukocytes, with 62 per cent polymorphonuclears. Under conservative treatment the patient improved, and she left the hospital three weeks later.

CASE 8.—*Stricture of the rectum, elephantiasis of the right labia and sloughing of the rectovaginal septum; colostomy; stricture of the left inguinal colostomy necessitating a second colostomy in the transverse colon.*

The patient was a Negro woman 36 years of age. She entered the hospital complaining of pain on defecation, blood and pus in the stools. Her blood pressure was 140 systolic and 100 diastolic. The patient stated that she had had a rectovaginal fistula since the birth of a child five years previously. Eighteen months ago she noticed that her stools were becoming smaller and defecation painful and that she had lost 16 pounds (7.3 Kg.) in weight. She had received a course of antisyphilitic treatment. On physical examination there was found an old laceration of the vaginal floor, extending down to the anterior rectal wall. Vaginal examination revealed a tender rectum that was filled with fecal material. On rectal examination a tight stricture ½ inch (1.27 cm.) above the internal sphincter was found. The Frei test elicited a positive reaction. A left inguinal colostomy operation was performed, at which time many adhesions were found around the sigmoid. Eighteen months later the patient was readmitted to the hospital, owing to cicatrization of her inguinal colostomy to such a point that it was necessary to perform a colostomy in the transverse colon.

The foregoing 3 cases illustrate some of the external manifestations that occur in association with strictures of the rectum in women.

CASE 9.—*Stricture of the rectum ruptured from bougie dilatation; recovery.*

A Negro woman 29 years of age was admitted to the hospital complaining of generalized abdominal pain. On the morning of admission the rectum was dilated by means of bougies in the outpatient department clinic. One-half hour after returning home she was seized with acute abdominal pain and vomiting. Examination showed blood pressure of 92 systolic and 60 diastolic. The abdomen was rigid and tender throughout. On rectal examination blood was found on the examining finger, and there was a stricture admitting the finger, which was tender on pressure. An emergency laparotomy was performed; this operation revealed a perforation of the rectosigmoid. A moderate amount of pus and fecal matter was found in the peritoneal cavity. A 1 inch (2.5 cm.) linear opening in the rectosigmoid was present, and the edges seemed slightly gangrenous. This was repaired by means of continuous silk sutures. Cecostomy was performed through a right gridiron incision, a mushroom catheter being used. The course was uneventful, and the patient was discharged two weeks later.

CASE 10.—*Stricture of the rectum and hemorrhage from instrumental dilation of stricture.*

A Negro woman 26 years of age entered the hospital complaining of bleeding from the rectum. The patient gave a history of constipation and rectal bleeding during the past year. On the day before admission she went to a local physician, who dilated the stricture, and she bled profusely on that day. On admission the patient had a pulse of 130, temperature of 94.4 F and blood pressure 112 systolic and 96 diastolic. On rectal examination she showed moderate bleeding of the rectum, with clots. The anal sphincter was relaxed, and the anal canal was filled with clots of blood. Under conservative treatment she was discharged nine days later, improved.

CASE 11.—*Stricture of the rectum, unsuccessful results with Jelk's operation and perforation of the rectum due to dilation with bougies; death, autopsy.*

The patient was a Negro woman 30 years of age.

First Admission.—There was a history of a rectal operation twelve years before admission, while eight years before admission she began to have difficulty in moving her bowels and passed blood at times; this difficulty had increased, and she began to pass pus per rectum and lost several pounds in weight during the past three months. Rectal examination showed thickened mucosa and a stricture 1½ inches (3.8 cm.) above the anal orifice. Six days after admission an incision was made through the ischiorectal fossa on each side, and by blunt dissection the perirectal exudate was broken up and freed from the rectal wall and the rectal wall was incised. There was also found at operation a second stricture 4 inches (10 cm.) above the anal margin, which would not admit the tip of the finger, and the perirectal exudate around this was broken up and the rectal wall was incised. A posterior proctotomy was also performed, and the patient was discharged fifteen days later, improved.

Second Admission.—Two and one-half years after the first admission the patient was readmitted. She had been receiving weekly dilations in a proctology clinic. The day before admission dilation was done with bougies, and severe pain developed in the abdomen and rectum. The pain was cramplike in character and increased in severity. She vomited twice. On admission her temperature was 100 F., pulse rate 100 and respiratory rate 20. The abdomen was slightly distended and exhibited tenderness and rebound tenderness, most pronounced in the left lower quadrant. An emergency laparotomy operation was performed, at which operation a perforation 1 cm. in diameter was found on the antimesenteric border of the sigmoid at a point 2 inches (5 cm.) proximal to the rectosigmoid junction. A thick purulent exudate was scattered over the pelvic organs and covered several loops of bowel. The sigmoid at the point of rupture was soft and was not thickened or indurated. A colostomy was performed through a left McBurney incision above the site of the wound. Culture from the abdomen at the time of operation revealed Escherichia coli. The patient died three days later.

Postmortem Findings.—Lungs: On section both lungs proved to be extremely congested and hyperemic, and a small amount of thin whitish fluid could be expressed on squeezing.

Abdomen: Located in the pelvis, surrounded by intestine, was a large abscess containing fecal-smelling purulent material. The intestine formed the superior wall of the abscess. The abdominal wall, fascia and parietal peritoneum consisted of a gangrenous slough, which extended from the lower midline incision to the left, involving the whole of the parietal wall, the diaphragm and the lumbar region, down to the pelvis.

Gastrointestinal Tract: Located approximately 8 inches (20 cm.) from the anorectal junction was a 1 inch (2.5 cm.) perforation, three fourths of which was repaired with chromic gut and the other one fourth of which was opened. For an area extending 10 inches (25 cm.) above the anorectal junction, the lumen of the rectum and rectosigmoid was narrow and showed flattening of the rugae. Surrounding the rectum was a large, firm mass, measuring about 10 cm. in diameter, which consisted of lipomatous tissue, with numerous white fibrous strands running through it. Located at the anorectal margin on the mucosal surface of the rectum were numerous fistulous tracts which had blind ends.

Gross Pathologic Diagnosis.—The following diagnosis was made: (1) perforation of the rectum, with pelvic abscess and gangrenous slough of the fascia and peritoneum of the anterior abdominal wall, diaphragm and lumbar region, (2) colostomy, (3) rectal stricture (lymphogranuloma inguinale), (4) perihepatitis and perisplenitis and (5) visceral congestion.

Microscopic Diagnosis.—The microscopic diagnosis was (1) acute peritonitis, (2) lymphogranuloma, (3) necrosis of the fascia of the abdominal wall, (4) perihepatitis and perisplenitis, (5) pulmonary edema and (6) visceral congestion.

The foregoing case is an example of Jelk's operation with unsuccessful results, because this patient returned two and one-half years later and died from perforation of the stricture.

CASE 12.—*Stricture of the rectosigmoid; death due to peritonitis from a ruptured diverticulum of the sigmoid; autopsy.*

A Negro woman 38 years of age was admitted to the hospital in coma. The history was obtained from her sister, who stated that she had had a rectal stricture for many years and had been receiving treatment for it privately during the past six months. Four days before admission she began to have frequent bowel movements and passage of a small amount of feces through the vagina and complained of abdominal pain and vomiting. Physical examination revealed a moribund Negro woman, who was pulseless and gasping for breath. Her abdomen was distended and tense. A Levine tube was passed, and an infusion of isotonic solution of sodium chloride and a blood transfusion were given at once. The patient died four hours later.

Postmortem Findings.—The peritoneal cavity contained about 300 cm. of an admixture of foul greenish brown fecal and purulent material. There were many fine adhesions between portions of the small intestine and the parietal peritoneum in the region of the incisional scar as well as at the cervical stump. Solid dark brown fresh fecal material was seen in the peritoneal cavity in the pouch made between the lower part of the sigmoid colon and the pelvic peritoneum.

Gastrointestinal Tract: The stomach and small intestines were grossly normal except for purulent coating. The colon was intact, but in the sigmoid portion in its terminal region were seen several fairly wide diverticula, measuring each approximately 2 by 3 cm. A mass was felt encircling the intestine at approximately the rectosigmoid junction. This mass was about the size of an orange and extended mainly as a posterior collar. On section this mass appeared as a palisaded, fairly firm, yellowish, fatty, fibrinous tissue and was completely encapsulated. In this region the sigmoid and rectum were both somewhat thickened and constricted, barely admitting one finger. Four centimeters above this constriction in the sigmoid, in the left anterolateral length, there was an elongated ragged ulceration, measuring 2.5 cm. in length, and extending from this in the pelvis, retroperitoneally as well as intraperitoneally, there was a large, soft mass of friable tissue, composed mainly of foul, dark brown, old fecal material surrounding the pelvic contents and extending also retroperitoneally in the left flank as far superiorly as the spleen. Anteriorly at the beginning of the anus there was a narrow double sinus tract communicating with the most anterior portion of the vagina.

Genitalia: The vagina appeared normal except for the fistulous tract in the extreme anterior portion.

Gross Pathologic Diagnosis.—The diagnosis was granuloma venereum with rectosigmoid stricture, rectovaginal fistula, diverticulosis of the sigmoid with rupture and extension, intraperitoneally and retroperitoneally, generalized peritonitis, septic liver, left interligamentous cyst, old parasplenitis with calcification and a healed hilar lesion of tuberculosis.

Cases 9 and 10 are cases showing some of the complications that may result from dilation with bougies in which the patients live. Case 11 proves that such dilations are not without danger. Case 12 is the first case that has been reported of a perforated diverticulum with death as a result of rectal stricture. David and Lauer cited a case of Phemister's in which chronic diverticulitis of the rectum resulted in extreme tubular constriction of the rectum. Phemister resected the rectum and the first part of the sigmoid in a youth, aged 20, who had a history of stenosis of the rectum for seven years. The resected rectum was in the form of a narrow tube. There were several diverticula in the rectum, the largest of which had an opening about 1 cm in diameter into the rectum and penetrated for about the same distance into the thickened rectal wall. Microscopic examination showed the rectal wall to consist of dense fibrous tissue with round cell infiltration.

CASE 13.—*Rectal stricture with thrombophlebitis of the left leg.*

A Negro woman 39 years of age entered the hospital with pain and tenderness of the left leg for the past three days. Her rectum had been dilated in our proctology clinic several times. On examination the left leg was edematous and tender. The temperature, pulse rate and respiratory rate were normal. Blood pressure was 140 systolic and 100 diastolic. The reaction of the blood was negative. On rectal examination she showed a tight stricture, which admitted the tip of the finger. The pain subsided, and the patient left the hospital thirteen days later improved.

(It has seemed rather remarkable to us that so few of these patients showed thrombophlebitis as a complication.)

CASE 14.—*Rectal stricture with hydrarthrosis of left knee joint; diabetes mellitus.*

The patient was a Negro woman 30 years of age.

Past History.—She had had inguinal adenitis on the right side ten years before admission. She had constipation and narrow stools for the past two years, with blood in the stool at times, together with loss of weight. Her left knee joint had been swollen and painful for the past two weeks. On physical examination a rectal stricture was found, which barely admitted the tip of the finger. The urine showed glucose (3 plus). Culture from the knee joint was sterile after forty-eight hours. The aspirated fluid was amber colored. The stricture was dilated with the patient under spinal anesthesia. The patient left the hospital one week later, without permission.

CASE 15.—*Stricture of the rectum and descending colon with polyarthritis.*

A Negro man 46 years of age entered the hospital with a history of pain in his joints. During the past three years he had diarrhea and bloody stools and lost 15 pounds (6.8 Kg.) in weight. On abdominal examination a mass the size of an

orange was felt to the left of the umbilicus, which was tender; the abdomen was soft, and ankles, wrists and elbows were swollen, hot and tender. Four days after admission he showed gross blood in his stools. Sigmoidostomy showed several small ulcerations of the rectum and 7 inches (17.7 cm.) above the rectum there was a stricture. The Frei test elicited a positive reaction. The Kahn test gave a 1 plus reaction. A barium enema showed pronounced diffuse narrowing of the descending colon and sigmoid and part of the rectum. The total protein content was 5.12 mg. per hundred cubic centimeters, albumin 2.69 mg., globulin 2.43 mg. and albumin-globulin ratio 1.2 mg. The patient left the hospital after receiving sulfonamide drugs, one week later, improved.

CASE 16.—*Stricture of the rectum with arthritis of the right hip joint.*

The patient was a Negro woman 42 years of age. Three years before admission the patient had an impassable stricture of the rectum. Her chief complaint was pain in the right hip joint and swelling of the right thigh, which had grown progressively worse. Examination showed a permanent artificial anus in the left lower quadrant. Rectal examination revealed an impassable stricture of the rectum. The right leg was swollen, tender and darker than the left. A roentgenogram showed a narrowing of the joint space of the right hip joint. The Frei test gave a strongly positive reaction. The patient remained in the hospital for one week and eventually remained under observation for three years, still complaining of her hip joint.

Cases 14, 15 and 16 are examples of arthritis of varying types which have occurred in this series of cases. Arthritis is not an uncommon manifestation of lymphogranuloma venereum.

CASE 17.—*Stricture of the rectum associated with bone changes.*

A Negro man 46 years of age had received rectal dilations and injections of Frei antigen in the clinic for many years. He had been to many hospitals, complaining of constipation and abdominal pain. On admission his temperature was 100 F., pulse rate 98 and respiratory rate 24. The patient showed a stricture of the rectum 2 inches (5 cm.) above the anus, obstructing the lumen. A biopsy specimen was taken from the stricture, and the pathologic report was lymphogranuloma venereum. Colostomy was done. Roentgenograms that were made of the spine and pelvis showed areas of rarefaction of the lumbar portion of the spine as well as of the pelvis. The patient had been admitted to the hospital three times, and he came into the hospital three years later with pneumonia of the lower lobe of the right lung, from which he died. Unfortunately, no autopsy was obtained.

The preceding case is one of osseous changes associated with lymphogranuloma venereum, which is relatively infrequent (figs. 11 *A* and *B*).

CASE 18.—*Rectal stricture, partial intestinal obstruction; no operation; recovery.*

A Negro woman 45 years of age entered the hospital with a history of vomiting for the past three weeks. Five years before she had a swelling of inguinal glands on the left side. Two years ago she noticed extreme constipation. She has had a poor appetite and has lost a considerable amount of weight during the past year, during which time her stools have been ribbon-like and occasionally blood streaked. Three months before admission constipation became severer, and she had colicky, epigastric pains. When examined the patient was a pale, emaciated, dehydrated

woman, with a distended tender abdomen. A rectal stricture was found, which did not admit the tip of the finger. The temperature, pulse rate and respiratory rate were normal. The blood cell count showed 3,980,000 red cells and 8,800 white cells, with a hemoglobin content of 70 per cent. The blood pressure was 150 systolic and 102 diastolic. She gave a positive reaction to the Frei test and a 3 plus reaction to the Wassermann test. Examination of the urine gave essentially normal results. A roentgenogram of her abdomen revealed distended loops of large and small bowels but no fluid levels. A barium enema showed a definite narrowing of the rectum, extending up to the lower part of the sigmoid, and above this point the sigmoid was distended. The patient was treated with high colonic irrigations and finger dilations, and she left the hospital ten days later, improved.

CASE 19.—*Rectal stricture with acute intestinal obstruction; colostomy; recovery.*

A Negro woman 31 years of age entered the hospital complaining of abdominal pain and vomiting. She had had abdominal pain for the past nine days, which at times was cramplike in character and at other times a constant distressing ache. The abdomen was distended and tender throughout. On vaginal examination the uterus was found to be retroflexed, and there was tenderness in both fornices. Digital examination of the rectum revealed a tight, impassable annular stricture 1½ inches (3.8 cm.) above the anus, with hard nodular edges. Conservative treatment was followed for three days, at the end of which time her vomiting continued and roentgenologic examination of the abdomen showed considerable gas in the large and small intestines, with fluid levels. Her reaction to the Kahn test was 4 plus. Colostomy was performed as an emergency measure. She left the hospital twenty days later, without permission.

CASE 20.—*Rectal stricture with acute intestinal obstruction; death; autopsy.*

A 70 year old Negro woman was admitted to the hospital, acutely ill and dehydrated. Her past history was that thirty-five years previously she had been operated on for a stricture of the rectum and that since that time she had been incontinent of feces. Four years after the first operation she was unsuccessfully operated on again to control her incontinence. Her present illness began the day before admission, at which time periumbilical pain developed and she vomited several times. Physical examination on admission revealed: The tongue was dry, the mucous membranes pale and the abdomen distended; there was no visible peristalsis and no palpable masses; the liver was not enlarged, and there was no rigidity or spasm of the abdominal muscles. The blood pressure was 140 systolic and 90 diastolic. Rectal examination showed a definite stricture 2 inches (5 cm.) above the anus, which did not admit the tip of the index finger. The temperature was 101.8 F., pulse rate 108 and respiratory rate 36. The red blood cell count was 3,700,000 and the white blood cell count 45,000, with 89 per cent polymorphonuclears. The hemoglobin was 70 per cent. A flat roentgenogram of the abdomen revealed distended loops of large and small bowels with fluid levels. Operation was advised, but it was refused by the patient. The patient was given supportive treatment, but she died ten hours after admission.

Postmortem Findings.—There was no consolidation of the lungs, although they were reddish purple and moderately anthracotic. The trachea and bronchi contained moderate amounts of frothy serosanguineous fluid. The tracheal and bronchial mucosa was diffusely congested. The heart was flabby and large and weighed 380 Gm. The aorta showed several irregular atheromatous plaques. The

colon and ileum were distended with gas and fluid. The wall of the rectum, about 8 cm. below the sigmoid flexure, felt indurated and somewhat pipe stemmed. No free fluid was present in the peritoneal cavity. The hepatic flexure of the colon was adherent to the gallbladder, and several bands of adhesions connected the first portion of the duodenum to the gallbladder. The rectum was strictured and admitted only the little finger. When the lumen was opened, the stricture was noted to extend for a distance of 16 cm. The mucosal folds were lost, and the mucosal surface appeared smooth, gray and fibrosed, almost hyalinized. Five centimeters above the anal rectal junction was an ulcerated area 1 by 0.5 cm. The ulceration was superficial, the edges were irregular and a small bony concretion was lodged in the floor of the ulcer at its lower pole. No hemorrhoids were present. The wall of the stricture felt moderately firm and indurated. On section a fairly smooth, gray, fibrotic surface was noted. Proximal to the stricture, the colon and practically the entire ileum appeared moderately distended with gas and dark brown fecal fluid. The serosal surfaces were grayish brown, and the serosal vessels were moderately injected. The distentions of the intestine diminished from the ileum to the jejunum, and in the latter segment of the bowel no distention was present. The mucosa of the distended intestine was fairly smooth and the villous folds almost completely absent. The stomach and duodenum were not unusual. No ulcerations of the small intestine were present.

Pathologic Diagnosis.—The diagnosis was acute intestinal obstruction due to rectal stricture caused by lymphogranuloma venereum, edema of the lungs, atherosclerosis of the coronary arteries and thoracic aorta, hypertrophy of the left ventricle, fibrosis of the mitral valve, cloudy swelling of the heart, liver and kidneys, diaphragmatic-hepatic adhesions, diaphragmatic-splenic adhesions, perisplenitis, arteriolosclerotic kidneys, atrophic ovaries and atrophy of the uterus, tubes and ovaries.

CASE 21.—*Rectal stricture with acute intestinal obstruction due to volvulus of the ileum; congenital elongated mesentery; postoperative pneumonia; death; autopsy.*

A Negro woman 59 years of age entered the hospital complaining of abdominal pain and vomiting. She had been constipated for many years, and, ten years before, she had had an operation for hemorrhoids. During the past months she had lost her appetite, lost weight and felt weak. Five days before admission, a pain developed in the epigastrium and she began to vomit. The next day she had a bowel movement, but there had been none since. On physical examination the patient was found to be an emaciated, acutely ill woman. On rectal examination an annular constricting mass which began 2 inches (5 cm.) above the anal verge and extended upward was found, but its upper limit could not be felt. The mass formed a stricture, which admitted only the little finger. The clinical diagnosis was acute intestinal obstruction due to stricture of the rectum. On the day of admission a duodenal tube was passed, and 2,000 cc. of fecal material gushed out. An infusion of isotonic solution of sodium chloride was given. A roentgenogram of the abdomen showed the small intestines distended with gas and the presence of fluid levels. An emergency laparotomy was performed, and at operation a loop of ileum several feet in length was found tucked under a segment of the mesentery. The portion of intestine proximal to the volvulus was distended, and the intestine below was collapsed. The volvulus was reduced and the abdomen

closed. The patient's temperature on admission was 100 F., and after the operation it rose to 104.6 F. and fell to 99 F.; it rose again to 104 F. just before death.

Laboratory Data on Admission.—The blood chloride level was 370. The Kahn reaction of the blood was negative. The white blood cell count was 28,000, with polymorphonuclears 89 per cent, and the red blood cell count was 5,100,000. The patient died seven days after operation. Death was due to terminal lobar pneumonia of the lower lobe of the right lung and edema of the middle lobe of the right lung and lower lobe of the left lung.

Autopsy Findings.—The serosal surface of the third portion of the duodenum, the jejunum and the proximal half of the ileum were grayish blue and gray, and the vessels were moderately injected. The mucosal surfaces were decidedly injected. The valvulae conniventes appeared edematous and congested. The mucosal surfaces of the colon were not flattened. When the rectum was opened, the mucosa showed several small superficial ulcerated areas extending from the anorectal junction proximalward for a distance of 6 cm. The mucosa was brownish gray, and the wall was moderately thickened and indurated. A few of the perirectal nodes were enlarged, pea sized and moderately firm. On section they had a homogeneous, pale gray, granular appearance. The final pathologic diagnosis was terminal lobar pneumonia of the lower lobe of the right lung, edema of the middle lobe of the right lung and lower lobe of the left lung, acute enteritis involving the third portion of the duodenum, jejunum and proximal half of ileum, congenitally elongated mesentery, rectal stricture, pronounced congestion and cloudy swelling of the kidneys (arteriosclerotic), cloudy swelling and fatty parenchymatous degeneration of the liver, atherosclerosis of the coronary arteries and thoracic aorta, multiple superficial ulceration of the esophagus (Levine tube) and decubitus ulcers of the sacral region and buttocks.

The foregoing 4 cases of intestinal obstruction of varying degree are typical of the commonest complication of rectal strictures. It is of interest to note that the most frequent and serious obstruction is in persons over 40 years.

CASE 22.—*Rectal stricture simulating ulcerative colitis.*

The patient was a Negro woman 28 years of age.

First Admission.—She entered the hospital with a history of frequent stools that numbered eight to twelve a day, containing blood and mucus, and pain in the left lower quadrant when she had a bowel movement. On physical examination a slight tenderness was noted in lower part of the abdomen. Inspection showed external hemorrhoids. Rectal examination showed a slight stricture with a granular, red mucosa. Sigmoidoscopic examination revealed acute and chronic ulceration as far as the sigmoidoscope would reach. The flat roentgenogram of the abdomen was normal. The Kahn reaction of the blood was negative. Cultures of the blood were sterile. No ova or parasites were found in the stool.

Second Admission (six months later).—The patient complained of vomiting, abdominal distention with attacks of diarrhea, chills and fever. A roentgenogram of the chest was normal. Repeated examination of the sputum was negative for tubercle bacilli. Examination of the rectum showed a well developed stricture, which barely admitted a tip of the index finger, with chronic ulceration above the strictured area. Colostomy was advised, but it was refused by the patient, who went home without permission.

CASE 23.—*Stricture of the rectum; colostomy followed by intrasphincteric amputation of the rectum (Pauchet's method).*

A Negro woman 38 years of age entered the hospital complaining of constipation, pain on defecation and discharge of pus through the rectum. She had had occasional vomiting and dizzy spells. Four years before admission she had been operated on for fistulas in ano. The blood pressure was 100 systolic and 72 diastolic. The red blood cell count was 1,500,000, the white blood cell count 7,800 and the hemoglobin content 76 per cent. The Wassermann test gave a 4 plus reaction. Studies of blood chemistry showed creatinine 1.1 mg., urea nitrogen 14.4 mg. and suger 78 mg. per hundred cubic centimeters. Temporary colostomy was performed. One month later the rectum was resected and the stricture excised, the sphincter being preserved according to Pauchet's technic, after which she was allowed to go home. Three months later she returned, and the spur was crushed and the colostomy closed. One month later she was discharged home, well.

Twenty-six cases in which this operation was used were reported by us in another article.[1e]

CASE 24.—*Stricture of the rectum and perforation of the rectum from rectal irrigation; death; autopsy.*

The patient was a Negro woman 25 years of age. The day before admission she had been struck over the head, following which she lost consciousness but quickly recovered. On admission the patient showed a hematoma of the forehead and left eye. Her past history was that she had had a fistula in ano since she was 13 years of age. Four years before, the patient was operated on for a pelvic condition, and since that time she had had pain on defecation and discharge from an anal fistula. The reaction to the Frei test was strongly positive. Rectal examination showed a scar above the anus resulting from a previous operation and a fistula to the left of the anus. A stricture was present ½ inch (1.2 cm.) from the anal verge, which admitted a finger. She was being treated in the hospital with rectal irrigation. Seventeen days after admission, after one of her rectal irrigations, she complained of severe abdominal pain and vomited three or four times. At that time the surgeon felt that there was a possibility of a perforation of one of the granulomatous areas following the irrigation. Two days later the abdomen was distended, tender and rigid, but she stated that similar episodes had happened before. A week later the diagnosis was peritonitis and pelvic infection, and the surgeon felt that the peritonitis was localizing and nonoperative. The patient died ten days later.

Autopsy Findings.—The abdomen was distended. The omentum was plastered down into the pelvis and over the small and large intestine. The loops of intestine were matted together by fibrous adhesions, which were fairly firm. In both abdominal troughs there was present a thick, creamy pus. This pus was also present under the diaphragm on the right side. The anterior surface of the right lobe of the liver was covered with a layer of fibrin and pus.

Gastrointestinal Tract: The mucosa of the small intestine was friable; however, no ulcerations could be made out, the friability being due to the peritonitis and pus in the wall of the blood vessels themselves, the pus due also to peritonitis. The large intestine was normal in appearance. At a point about 8 inches (20 cm.) from the rectum the mucosa of the rectum and sigmoid became thickened and had a grayish color. The mucosa lay in folds in places and looked like

the tentacles on a squid. Multiple strands of fibrous tissue ran through the mucosa, the entire wall was thickened and narrowed and the lumen was constricted. Near the rectum there were two large ulcerations, each about ½ inch (1.2 cm.) in diameter. The bases of the ulcers were necrotic, and in the centers of the ulcers were small openings, which were ¼ inch (0.6 cm.) in diameter, which opened into the tissue in back of the rectum.

Reproductive Organs: The rectovaginal wall was thickened and infiltrated. Both tubes were distended and contained pus. The left ovary was normal, and the right ovary could not be located.

Spleen: The spleen was enlarged to about three times its normal size and was septic in appearance.

Anatomic Diagnosis.—The diagnosis was lymphogranuloma inguinale, stricture of the rectum, ulcerative proctitis, congestion and edema of the lungs, ecchymosis of the left eyelids and fistula of the rectum.

Cause of Death.—The cause of death was lymphogranuloma inguinale, stricture and ulcer of the rectum and acute suppurative peritonitis.

CASE 25.—*Rectal stricture, rectovaginal fistulas, anal fistulas, duodenal ulcers, esophageal varices; colostomy; death from pneumonia.*

The patient was a Negro woman 49 years of age.

First Admission.—She entered the hospital complaining of abdominal pain. She gave a history of having had a colostomy performed in a hospital in Connecticut for what she was told was a growth in the rectum, before which time she had extreme constipation. Her reaction to the Frei test was positive. On admission she complained of abdominal pain and, in spite of her colostomy, a discharge of her fecal material through the vagina when she had a bowel movement through the rectum, which was two or three times a day. She was advised to have a colostomy in the transverse colon but refused.

Second Admission.—One year later she was admitted to the medical service because of pain in the right side of the chest, cough and chills. Six weeks prior to admission she had been in bed because of generalized weakness. Her blood pressure was 78 systolic and 60 diastolic, the pulse rate was 120 and the respiratory rate 28. There was tenderness over the lower lobe of the right lung and impaired resonance posteriorly. Roentgenograms showed pneumonia of the right middle and lower lobes of the right lung. Type III pneumococci were obtained from the sputum. The patient was treated with sulfadiazine and died three days later.

Autopsy Findings.—There was present a colostomy in the left lower quadrant, which barely admitted the tip of a small finger.

Lungs: The entire right lung was completely consolidated, hard and dull gray, except for the apical tip. The cut surface revealed a uniform grayish consolidated appearance, with a purulent discharge exuding from the bronchi.

Abdomen: The lower end of the esophagus contained three or four dilated varices, one of which was thrombosed. The first part of the duodenum contained an elliptic-shaped ulcer about 1 cm. in diameter, with a ragged edge and a granular base. The surrounding area was somewhat indurated, and there were four smaller ulcerated areas in the vicinity about 2 mm. in diameter, with the edges thickened and indurated. The rectum was dark red and congested but not stenosed or strictured. However, the perirectal tissues were decidedly indurated and thickened,

and the anal canal contained numerous fistulous tracts opening up into the external anal area. The mucous membrane of the rectum and the anal canal was hemorrhagic.

Liver: The liver was enlarged, and the right lobe contained a fibrinous exudate over the capsule.

The gross pathologic diagnosis was lobar pneumonia of the lower, middle and upper lobes of the right lung, confluent bronchopneumonia of the lower lobe of the left lung, varices of the esophagus, multiple chronic duodenal ulcers, lymphopathic disease of the rectum with a waterpot anal fistula and old sigmoid colostomy.

(This case illustrates the debilitating effects of a rectal stricture, which undoubtedly was the major predisposing cause of her fatal pneumonia.)

CASE 26.—*Stricture of the rectum, perineal resection of the rectum; recovery.*

The patient was a Negro woman 26 years of age, who had a colostomy for a rectal stricture three months before she was admitted to the hospital. Multiple scars were present over the buttocks from abscesses resulting from the stricture. Perineal resection of the rectum was done, and all diseased tissue was excised. The rectum was found strictured throughout its extraperitoneal length. The healthy rectal mucosa was sutured to the skin, with the sphincter preserved. Pathologic examination of the excised rectum gave the following diagnosis: lymphogranuloma venereum of the rectum, showing giant cells, plasma cells and focal and round cell infiltration. The patient was discharged from the hospital one month later.

CASE 27.—*Stricture of the rectum, urethral stricture.*

The patient was a Negro man 46 years of age. For the past year he received treatment for urethral strictures; at the same time he noticed severe constipation, pain on defecation and a purulent discharge from the perianal area. A urethral stricture was found to be present, which with difficulty admitted a size 20 French sound. Several pinpoint openings were present in the perineum, and from each opening there was a discharge of purulent material. One inch (2.5 cm.) above the sphincter there was a stricture, which admitted only the tip of the examining finger. The patient remained in the hospital five days and left without permission.

SUMMARY

Strictures of the rectum due to lymphogranuloma venereum are a serious threat to life in some instances. Negro women are chiefly affected. Some conditions are mild and seem to cure themselves. Other conditions progress in spite of all known methods of treatment. It is our opinion that these variations in clinical behavior result from the fact that there are different strains of the virus and that the virus produces a reaction according to the host. The early diagnosis and treatment in all cases is important. In the prestricture stage sulfonamide compounds seem to have some value, but there is a question as to whether sulfonamide drugs can prevent permanently an extension of the processes in some cases. It is likewise true that in some of the instances in which sulfonamide drugs seem to have been of value the evidence is not conclusive as yet that these patients might not have done as well without the sulfonamide compounds as far as checking the activity of the virus is concerned. Sulfonamide drugs do help in clearing up the

secondary superimposed infections that are present in these cases and thus improve the condition of the patient clinically. Penicillin has proved valueless in our hands. Once a fibrous stricture has occurred, drugs are of value only by elimination of the toxic effect of secondary bacterial invasion due to the fact that the blood supply to and through the dense scar tissue is so lessened that no adequate therapeutic concentration of the drug is possible.

Some conditions do not progress rapidly and are not serious, while other conditions do progress rapidly in spite of all forms of treatments, with the exception of early excision. Colostomy helps many patients (1) by lessening secondary infection and (2) by overcoming the toxic effects of chronic obstruction of the bowel. Surgical treatment alone is of value once a fibrous stricture of any considerable extent is developed. Warthen's obliteration of the cul-de-sac operation offers the possibility of lessening the complications that are inherent in colostomies, namely, anterior grade and retrograde herniation. It cannot, however, prevent stenosis of the colostomy opening, which occurs in many instances. Pauchet's excision operation or a modification thereof at this time offers the best method of cure for strictures low in the rectum. This does not exclude the sacroperineal excision operation of Hartmann. These operations are of such magnitude that they should be performed only by experienced surgeons. When the disease involves the entire rectum or is high in the rectum, involving the rectosigmoid area, abdominoperineal extirpation is indicated if the patient's clinical condition does not improve after colostomy. In the rare cases in which the descending colon is involved, a permanent artificial anus in the transverse colon should be made. Carcinoma occurs as a superimposed factor in a sufficiently large number of cases to be of clinical significance.

Much further study is needed to complete our knowledge and understanding of this subject.

APPENDICITIS

A Review of Nine Hundred and Thirty-Six Cases at the Cincinnati General Hospital

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CINCINNATI

IN TWO previous reports from this clinic, all cases of patients with appendicitis admitted to the Cincinnati General Hospital between 1915 and 1934 [1] and 1934 and 1939 [2] respectively were reviewed. The present study is a continuation of this series and will include all cases of patients with appendicitis treated between Jan. 1, 1939 and Jan. 1, 1944.

In the preceding articles the general trend toward a reduced mortality rate from appendicitis as seen in this hospital was noted. This favorable trend was attributed to (1) the adoption of the McBurney incision in 1922 for appendectomy and (2) the intensive educational campaign concerning management of appendicitis directed toward physicians and the public. This campaign, fostered by the Public Health Federation and the Academy of Medicine of Cincinnati, is still in progress. The sustained and commendable improvement resulting from the campaign may be gaged by a comparison of certain phases of the morbidity and mortality statistics of the present review with those in the preceding articles in this series.

An attempt will be made in this paper to consider certain aspects of the syndrome and treatment of appendicitis in a manner comparable to that employed in the earlier studies. It is not the purpose to uncover new facts concerning appendicitis or its treatment. In bringing to date a study of all cases of patients with appendicitis treated in a large clinic for twenty-nine years, we are advancing toward the objective which was selected when this series of papers was begun. It is our belief that this article and those which precede and will succeed it may serve as references of some value in the presentation of a reasonable, comprehensive concept not only of the general trends in the management of appendicitis but of the various aspects of the disease itself.

From the Department of Surgery, University of Cincinnati College of Medicine and the Cincinnati General Hospital.

1. Reid, M. R.; Poer, D. H., and Merrell, P.: A Statistical Study of 2,921 Cases of Appendicitis, J. A. M. A. **106**:665 (Feb. 29) 1936.

2. Reid, M. R., and Montanus, W. P.: Appendicitis: An Analysis of 1,153 Cases at the Cincinnati General Hospital, J. A. M. A. **114**:1307 (April 6) 1940

PATHOLOGIC CLASSIFICATION

The classification of appendicitis based on clinical and pathologic findings is in accordance with that outlined in the previous papers of the series.[3] The 936 cases in this report were grouped as follows: 605, or 64.6 per cent, were classified as acute appendicitis without perforation; 260, or 27.7 per cent, as acute appendicitis with perforation, and 71, or 7.6 per cent, as chronic or interval appendicitis. Of the 260 cases of acute appendicitis with perforation, 167, or 17.8 per cent

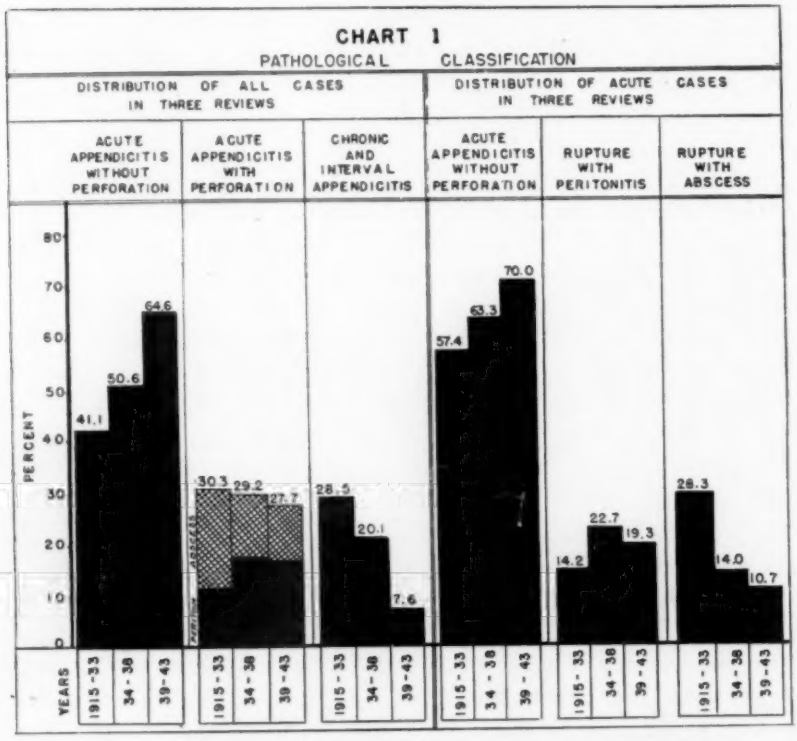

Chart 1.—Pathologic classification of cases of appendicitis.

of the entire series, were classified as acute appendicitis with perforation and generalized peritonitis. The remaining 93, or 9.9 per cent, were classified as acute appendicitis with perforation and abscess. The preceding data, with corresponding statistics for the earlier studies, is presented in chart 1.

The pronounced reduction in the total number of cases (936) as compared with 1,153 cases in the preceding five year period [2] is explained by the decreased census of charity hospitals since 1941. For example, 1,789 major operations were performed in this institution

3. Reid, Poer and Merrell.[1] Reid and Montanus.[2]

in 1943, as compared with 2,232 in 1939.[4] A similar observation was made by Hathaway[5] in 1943.

It may be noted that the incidence of chronic and interval appendicitis in this study is at pronounced variance with that of the preceding reviews. The discrepancy is explained by the elimination in the present series of (1) all cases in which a diagnosis of mesenteric adenitis was made at operation, (2) all cases in which signs and symptoms attributed to chronic or interval appendicitis were not relieved by operation and (3) all cases in which the diagnosis of chronic or interval appendicitis was not substantiated by microscopic examination of the appendix. It would be fitting to reflect that the reduced number of cases of chronic and interval appendicitis in this series results in a corresponding relative increase in the percentage of perforations. A more accurate interpretation may be obtained by the comparison of the proportion of perforations among patients with acute appendicitis, referred to in chart 1.

AGE

The average age of all patients in this series was 25.9 years. The decade of highest incidence was that in the years between 11 and 20 (355 cases), while the decade of next highest incidence was that in the years between 21 and 30 (241 cases). Perforation of the appendix followed a similar distribution, 74 and 42 cases in the second and third decades respectively. These observations are in accord with the preceding articles in this series and with recent reviews from other clinics.[6]

It would seem unnecessary to repeat that appendicitis is primarily a disease of youth and that in 107 of the 260 cases of perforation in this series the patients were under 21 years. A rather startling finding in this study, however, was the occurrence of 83 perforations, an incidence of 58 per cent, in the 142 cases of acute appendicitis in patients over 40 years, a finding explained in part by the knowledge that appendicitis in the more advanced age groups may present an atypical syndrome or problems in differential diagnosis not encountered in younger patients. It was interesting to note that the departure of large numbers of young men to the armed forces was not a factor in the decreased census. It was found that the relative incidence of appendicitis among patients in the second or third decades of life varied less than 5 per cent during any of the five years reviewed.

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4. Annual Report of the City Manager, Cincinnati, Ohio, 1943.

5. Hathaway, H. R., and Watkins, R. M.: Economic State and Mortality in Appendicitis, Ohio State M. J. **39**:247 (March) 1943.

6. (*a*) Jennings, J. E.; Burger, H. H., and Jacobi, M.: Acute Appendicitis: A Clinical and Pathological Study of 1,680 Cases, Arch. Surg. **44**:896 (May) 1942. (*b*) Busch, I., and Spivack, A. H.: Observations on Acute Appendicitis: A Series of 635 Cases, Surg., Gynec. & Obst. **70**:241 (Feb.) 1940.

SEX

In the present study the well known preponderance of appendicitis in the male is again demonstrated. Of the total of 936 cases, 619, or 66.1 per cent, were in males and 317, or 33.9 per cent, in females. The incidence of perforation in acute appendicitis was 196, or 31.6 per cent, in males, and 64, or 20.1 per cent, in females.

SEASON

Unlike the preceding review, in which there was an increase of appendicitis in the summer, the greatest seasonal incidence in this series was during the winter months. Two hundred and seventy-three of the 936 patients were admitted during the first three months of the year.

RACE

The race distribution paralleled that of the hospital census. Six hundred and ninety-two, or 73.9 per cent, of the patients were white, while the remaining 244, or 26 per cent, were Negroes. The incidence of perforation among patients with acute appendicitis in the present series was 173, or 27.2 per cent, among white patients and 87, or 38.2 per cent, among Negroes.

DELAY IN HOSPITALIZATION

In the previous reviews from this clinic emphasis was placed on the danger attending delay in the seeking of hospitalization for acute appendicitis. It is believed that the campaign to educate the public regarding the syndrome of acute appendicitis has resulted in progressive reduction of the average period between onset of symptoms and hospitalization. We are pleased to report that there has been an additional decrease. The average period between onset of symptoms and hospitalization in the group of patients with acute unruptured appendicitis was 26.6 hours as compared with the mean of 33.1 hours recorded for the preceding five years. In the group classified as acute appendicitis with perforation and generalized peritonitis, the average time elapsing between onset of symptoms and admission was 54.3 hours (64.9 hours in the 1934-1938 series). In patients with perforation and abscess formation, the average elapsed time was 116.5 hours, against 145.9 hours in the 1934-1938 review.

The mean delay in hospitalization for all patients with acute appendicitis was 41.7 hours (chart 3). The figure compares favorably with the average delay in hospitalization (thirty-seven hours) reported by Hathaway and Watkins [5] in their series, since 76 per cent of their patients were admitted to private hospitals. These authors observed that in 1940 and 1941 "staff patients" sought attention on an average of nine hours later than private patients.

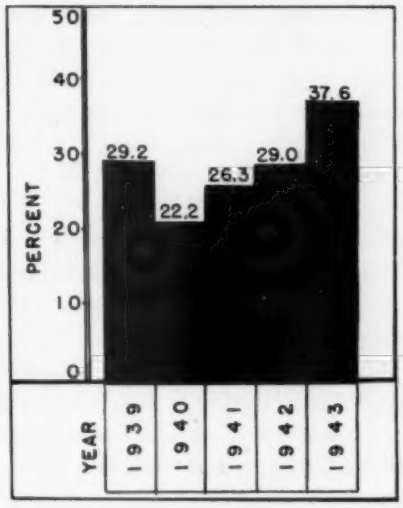

Chart 2.—Incidence of perforation among all cases of appendicitis at the Cincinnati General Hospital in the period 1939-1943.

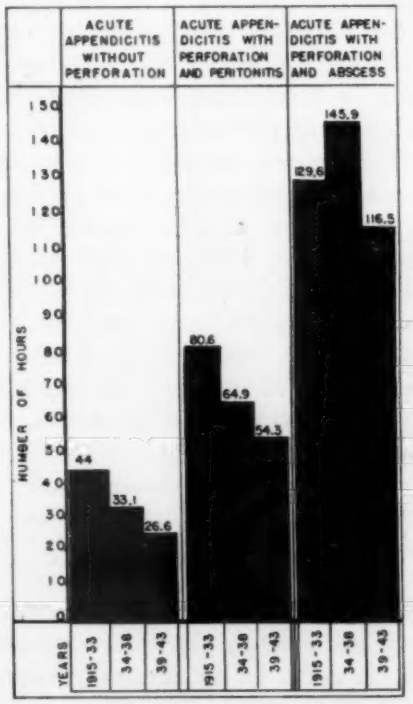

Chart 3.—Time in hours between onset of symptoms and hospitalization.

It is probably worthy of note to compare the elapsed time between onset of symptoms and admission among white patients and Negroes. In all groups, Negro patients were admitted to the hospital at a significantly later hour than white patients (table 5). The relation between elapsed time between onset and admission and mortality rate will be discussed in subsequent paragraphs.

CATHARTICS

The earlier articles from this clinic stressed the deplorable use of laxatives prior to hospital admission and described the campaign of education by which the public was informed of the dangers of self medication for abdominal complaints. It is gratifying to find that there has been improvement as regards this phase of the study. Whereas in the 1934-1938 series of 921 patients with acute appendicitis "410, or 44.5 per cent, gave a history of having taken some cathartic," [2] in this series of 865 cases of acute appendicitis, 329, or 38 per cent, of the patients were known to have taken such medication. This is a decrease of 6.5 per cent. The correlation between catharsis and perforation stressed in this clinic and by others [7] is again shown on examination of the totals. Of 605 cases of acute appendicitis without perforation, in 189, or 31.3 per cent, the patients had taken laxatives, as compared with 140, or 53.8 per cent, of the 260 cases of acute appendicitis with perforation in which there was a history of catharsis.

An interesting aspect of catharsis is found in a comparison of the use of medication by the Negro and white races. Of 141 Negroes with acute appendicitis wihout perforation, 64, or 45.4 per cent, took laxatives, as compared with 135, or 27.2 per cent, of the 464 white patients with similar condition. The difference was less pronounced among cases of acute appendicitis with perforation, the figures for the respective races being Negro 58.3 per cent and white 51.4 per cent. The most commonly used preparations were magnesium sulfate (102 cases) and castor oil (52 cases). The Negro patients used these two preparations almost twice as frequently as did white patients, 31.2 per cent using them against 16.8 per cent of all patients suffering with acute appendicitis respectively. Among 8 cases in which cathartics were known to have been prescribed by physicians, there were 6 perforations, of which 1 was fatal.

CLINICAL DATA

The various physical findings and symptoms occurred with much the same frequency as noted in the preceding reviews. Thus in 865

7. (*a*) Reynolds. J. T.: Symposium on Abdominal Surgery. Appendicitis: Basic Considerations in Choice of Therapy, S. Clin. North America **24**:128 (Feb.) 1944. (*b*) Footnote 6.

cases of acute appendicitis abdominal pain occurred in 861, or 99.5 per cent, nausea was noted in 363, or 41.9 per cent, and emesis occurred in 581, or 67.1 per cent, while rectal tenderness was noted by the physician in 534, or 61.4 per cent.

If one assumes that the syndrome of acute appendicitis is frequently characterized by pain, nausea, emesis and rectal tenderness, it could be stated that any patient in whom were noted at least three of these signs and symptoms presented the classic picture of appendicitis. It should be pointed out that only 536, or 61.9 per cent of the 865 cases of acute appendicitis may be said to have presented such characteristic clinical pictures.

LABORATORY DATA

The mean temperature of all patients with acute appendicitis was 99.9 F. Of the patients with acute appendicitis without perforation the average temperature was 99.5 F., while in the group of patients with acute appendicitis with perforation the mean temperature was 100.8 F. The average white blood cell count in all cases of acute appendicitis was 15,800, whereas in the groups of cases classed as acute appendicitis without rupture and acute appendicitis with rupture the mean white blood cell counts were 15,100 and 17,400 respectively.

ANESTHESIA

Anesthesia for appendectomy was again chiefly of the inhalation type. At the time of the last review from this clinic it was "our policy to use nitrous oxide-ether anesthesia when operating on patients with appendicitis." [2] Since the last report, cyclopropane has been used with increasing frequency; thus in 1943 that agent was used for 48.2 per cent of all patients with appendicitis receiving inhalation anesthesia. Spinal anesthesia, used in 13 per cent of all cases, was given formerly in cases "in which general anesthesia was contraindicated." [2] Recently, however, spinal anesthesia has been used for an appreciable number of patients who formerly would have received inhalation anesthesia. Local anesthesia alone or supplemented with other agents was used in a small number of "poor risk" patients (10 cases in all).

INCISIONS

In this clinic the McBurney incision is the customary approach to the appendix for reasons which were presented in the initial paper [1] and which are worth repetition: ". . . acute appendicitis can be adequately treated through the McBurney approach, whether it is an unruptured appendix, an appendiceal abscess or peritonitis. Operations so performed are less severe, and postoperative complications such as obstruction, broken-down wounds and ventral hernias are less common. Adequate drainage is more easily and safely secured through a McBurney

incision." In the cases in which there is a question of differential diagnosis between appendicitis and another condition, as cholecystitis, pancreatitis, Meckel's diverticulitis or a twisted ovarian cyst, a McBurney incision is made deliberately, in the belief that no harm will be done should an additional incision be necessary for the management of any other condition. In the cases of questionable diagnosis, the abdomen is draped so that a supplementary laparotomy incision can be made without confusion. In spite of the excellent results with the right rectus incision, reported by Ladd and Gross [8] and Busch and Spivak,[6b] Jennings and colleagues [6a] and Brett and Watkins [9] reported equally convincing results with the McBurney incision.

In the 923 patients on whom operation was performed, the McBurney incision was employed 899 times, the right rectus approach 18 times, a cul-de-sac drainage of a pelvic abscess twice and the Rockey incision twice. In 1 patient, a ruptured appendix with abscess formation was encountered in the sac of a strangulated femoral hernia approached through an inguinal incision. In the final case, the diagnosis was incorrect and a Hoag incision was made.

It is a notable fact that hernias did not occur in any McBurney incisions which were closed, whereas when such incisions were drained there were 8, or an incidence of 0.9 per cent, of 899 patients whose incisions were at this site. Of 18 cases of right rectus incisions, hernias developed in 2, an incidence of 11.1 per cent. In 10 cases of McBurney incisions with Weir extensions, there were 2 cases of evisceration and 3 of hernia. All the incisions were drained. Evisceration in the McBurney incisions was confined wholly to those with Weir extensions. This was 0.12 per cent, as compared with 0.65 per cent for all abdominal incisions [10] over a ten year period.

SURGEONS

The operations in this series were performed by thirty-nine surgeons, twenty of whom performed ten or more appendectomies.

CONSERVATIVE THERAPY

Conservative therapy in acute appendicitis with perforation has never been recommended at this clinic, although championed by others.[11] Thus, of 13 patients treated conservatively, 4 died after being admitted

8. Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infants and Children, Philadelphia, W. B. Saunders Company, 1941, p. 840.

9. Brett, J. D., and Watkins, R. M.: McBurney Incision in Appendicitis, Ohio State M. J. **39**:140 (Jan.) 1943.

10. Tashiro, S.: Wound Disruption: A Study of 55 Cases at the Cincinnati General Hospital, Surg., Gynec. & Obst. **78**:487 (May) 1944.

(Footnotes continued on next page)

in terminal condition and 1 refused operation and recovered, while in 8 cases a resolving abscess was not drained although appendectomy was subsequently performed three to six months later.

In 32 cases appendectomy was not performed, in spite of exploratory operation, because the presence of the appendix in or beyond the confines of a well walled-off abscess precluded its removal. Six of the patients were readmitted for subsequent operation for interval appendicitis, and 1 returned after several months with acute appendicitis with perforation and generalized peritonitis.

DRAINAGE

In an earlier article, our views at that time concerning drainage in acute appendicitis with perforation were discussed at some length and can be summarized in this excerpt: ". . . unless extensive necrosis or actual fecal contamination of the peritoneal cavity is present it is better to close the peritoneum and drain the wound down to it."[2] Among the arguments for such a procedure are (1) wounds in which the peritoneal cavity has been drained are prone to hernias,[12] (2) drains form a portal of entry for infection from without, (3) drains are foreign bodies and may stimulate adhesions, which may result in intestinal obstruction, and (4) the obtaining of drainage from remote portions of the peritoneal cavity by drains [13] is unlikely.

The findings of the second and present reviews may force us to modify our previous policy. Granted that drains which are placed customarily in the pelvis and the right paravertebral gutter will not allow the escape of pus from more distant portions of the abdominal cavity, there is clinical evidence to show that an avenue has been established for the escape of pus localized at or contiguous to the areas in which the drains are placed. Thus in several cases it has been a satisfaction to observe subsidence of severe abdominal signs and symptoms as large quantities of exudate escaped from the drainage tract at the time of or even several days after the removal of the drains.

In the consideration of the complication of pelvic abscess, it has been noted that this condition occurs with greater frequency in the cases in which the peritoneum is closed and only the wound drained than in those in which the abdominal cavity is drained. Of 58 cases of

11. Ochsner, A., cited by Reynolds, J. J.: Conservative Management of Appendiceal Peritonitis, New Orleans M. & S. J. **87**:32 (July) 1934. Adams, J. M., and Bancroft, P. M.: The Conservative Management of Appendiceal Peritonitis in Children, J. Pediat. **12**:298 (March) 1938. Reynolds.[7a]

12. Cave, H.: Incidence and Prevention of Incisional Hernias, J. A. M. A. **101**:2038 (Dec. 23) 1933.

13. Meleney, F. L., and Howes, E. L.: Disruption of Abdominal Wounds with the Protrusion of Viscera, Ann. Surg. **99**:5 (Feb.) 1934.

acute appendicitis with perforation in which the incisions were drained to the peritoneum, pelvic abscesses developed in 14, or 24.1 per cent, whereas this complication developed in only 21, or 12.1 per cent, of the 174 cases in which the peritoneal cavity was drained. In the 1934-1938 series the corresponding percentages were 12.73 and 9.1 respectively. On the other hand, in this series there remains a noticeable discrepancy in the mortality rate in the cases in which the incisions were drained down to the abdominal cavity and those in which the peritoneal cavity was drained, the respective mortality rates being 8.6 per cent and 12.1 per cent. In the preceding review a corresponding comparison was 9.1 per cent and 16.2 per cent respectively. It must be emphasized that drainage of the peritoneal cavity was dependent on the amount of "contact necrosis" and "fecal contamination."

Of 11 patients with acute appendicitis with perforation and peritonitis whose wounds were closed without drainage, infections developed in the incision in 7, or 63.8 per cent. There were in all 8 patients with appendicitis with perforation and abscess formation whose incisions were closed and in whom no complications arose. The remaining 9 patients with appendicitis with rupture were treated conservatively (table 1).

TABLE 1.—*Management of Wounds in Cases of Ruptured Appendixes*

	Number of Cases
Drainage of wound	58
Drainage of peritoneal cavity	74
Closure without drainage	19
Conservative treatment	9

In 25 cases of acute appendicitis without perforation drains were placed down to (8 cases) or into the peritoneum (17 cases) for various reasons, such as bleeding, contamination and suspected bacterial perforation. Pelvic abscesses did not occur in this group.

BACTERIOLOGY

Any exudate encountered in the peritoneal cavity at operation is cultured. The number of positive cultures and the varieties of organisms obtained were disappointing but not unexpected. Because of unavoidable curtailments in personnel, plating of swabs has been frequently delayed, with the result that many cultures which obviously should have been positive under normal conditions have been negative. Altemeier [14] has shown that a large number of the organisms recovered from the peritoneal cavity in cases of peritonitis are of the anaerobic type. During

14. Altemeier, W. A.: The Pathogenicity of the Bacteria of Appendicitis Peritonitis, Surgery **11**:347 (March) 1942; Surgical Infections of the Peritoneum, S. Clin. North America **22**:437 (April) 1942.

much of the period reported on in this study, the routine failed to provide for culture of this group of organisms.

DURATION OF HOSPITAL STAY

The average duration of hospitalization of patients with acute appendicitis without perforation was 9.25 days. The mean duration of hospitalization for patients with perforation and generalized peritonitis and perforation with abscess formation was 21.6 and 22.7 days respectively.

TABLE 2.—*Complications in Cases of Appendicitis*

	Chronic or Interval	Acute Without Perforation	Perforation and Peritonitis	Perforation and Abscess	Total
Atelectasis	0	4	7	1	12
Reaction to blood transfusion	1	0	1	0	2
Generalized peritonitis	0	1	..	2	3
Pulmonary edema	0	0	2	2	4
Paroxysmal tachycardia	0	0	0	1	1
Uremia	0	0	0	2	2
Retroperitoneal abscess	0	0	0	1	1
Cervical adenitis	0	1	0	0	1
Sinus in wound	0	0	2	2	4
Keloid	1	4	2	1	8
Acidosis	0	0	1	1	2
Erysipelas	0	1	0	0	1
Psychoneurosis	0	0	0	1	1
Paronychia	0	0	0	1	1
Gangrene of ileum	0	0	1	0	1
Portal thrombophlebitis	0	0	1	0	1
Acute hemorrhage from cecum	0	0	1	0	1
Subphrenic abscess	0	1	7	1	9
Pulmonary congestion	0	0	0	1	1
Pelvic abscess	0	0	30	8	38
Subhepatic abscess	0	1	0	1	2
Thrombophlebitis	0	1	3	2	6
Fecal fistula	0	0	5	3	8
Otitis media	0	1	1	0	2
Empyema	0	0	4	0	4
Acute toxic leptomeningitis	0	0	1	0	1
Wound infection, clean patients	0	18	0	0	18
Wound infection, dirty patients	0	0	16	4	20
Liver abscess	0	0	1	0	1
Evisceration	0	1	1	0	2
Hernias	0	3	8	2	13
Jaundice	0	4	8	4	16
Pleural effusion	0	0	5	0	5
Thyroid crisis	0	1	0	0	1
Acute cholecystitis	1	0	0	0	1
Dermatitis venenata	0	3	0	0	3
Lobar pneumonia	0	0	1	0	1
Complications in urinary tract	0	4	1	1	6
Cerebral accident	1	0	0	0	1
Soft tissue abscess	0	4	1	1	6
Acute exacerbation rheumatic valvulitis	1	0	0	0	1

COMPLICATIONS

As was done in the preceding survey, we content ourselves with listing the complications occurring with the various types of appendicitis, since there is no space for detailed discussion and no unusual conditions were encountered (table 2).

MORTALITY

In accordance with the second paper of the series [2] the mortality statistics are based on all cases of appendicitis rather than on the operative cases, as in the initial study. The total number of deaths in the present series of 936 cases was 31, or 3.3 per cent, as compared

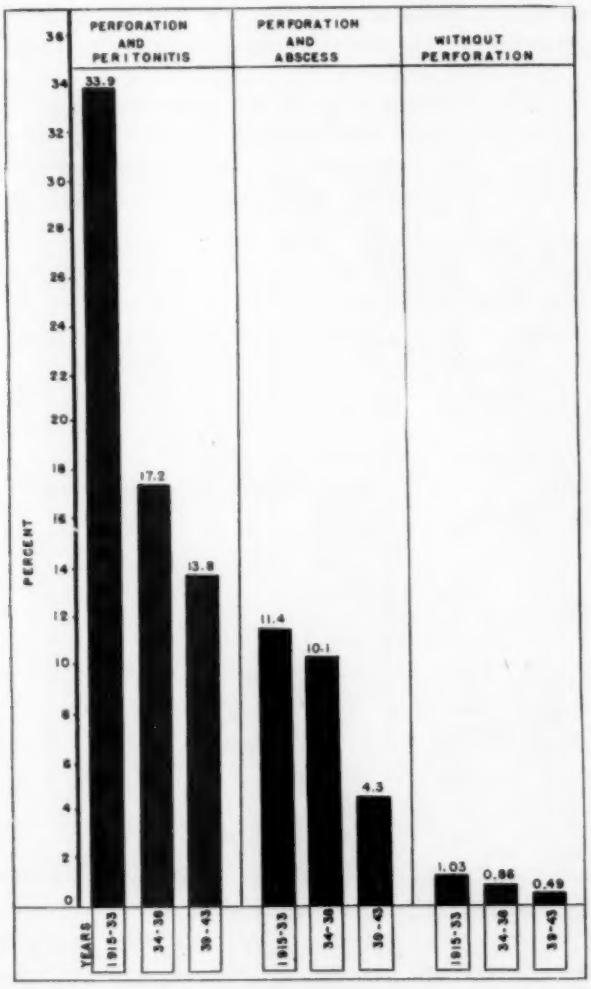

Chart 4.—Fatality rate in cases of acute appendicitis.

with 6.4 per cent and 4.86 per cent in the earliest and second reports respectively. In the group of cases classified as chronic or interval appendicitis, there was 1 death in 71 cases, a mortality of 1.4 per cent. The nature of the man's death (cerebral thrombosis) can hardly be ascribed to appendicitis. There were 3 deaths, 0 49 per cent, in the

group classed as acute appendicitis without perforation, against percentages of 0.86 and 1.03 for the first and second reviews.

In the group of 167 cases designated acute appendicitis with perforation and generalized peritonitis, 23, or 13.77 per cent, of the patients died, as compared with the respective figures 33.9 per cent and 17.2 per cent for the 1915-1933 and 1934-1938 series. Only 4, or 4.3 per cent, of 93 patients suffering with perforation and abscess formation died, in comparison with 11.4 per cent and 10.1 per cent for the first and second studies (chart 4).

TABLE 3.—*Mortality Based on Time Elapsed Between Onset of Symptoms and Admission*

	Total Cases	Deaths	Per Cent
0 to 48 hours	659	14	2.1
49 to 72 hours	97	4	4.1
73 to 96 hours	30	3	10.0
4 to 6½ days	41	6	14.6
6½+ days	34	3	8.8

The highest mortality occurred in the patients who delayed hospitalization. Thus, if the period between onset of symptoms and admission to the hospital is divided into five arbitrary groups, 2.1 per cent of the 639 patients who entered the hospital within forty-eight hours after the onset of symptoms died, whereas 10 per cent of the patients who

TABLE 4.—*Mortality and Cause of Death*

Type of Appendicitis	Number of Cases	Total
Chronic and interval		1
Cerebral accident	1	
Acute unruptured		3
Thyroid crisis	1	
Generalized peritonitis	1	
Death from anesthetic	1	
Acute with perforation and peritonitis		23
Generalized peritonitis	17	
Peritonitis and lobar pneumonia	1	
Peritonitis and bronchopneumonia	1	
Peritonitis and perforation of ileum	1	
Bronchopneumonia	1	
Septicopyemia	1	
Intra-abdominal abscesses (empyema)	1	
Acute with perforation and abscess		4
Pulmonary edema	1	
Generalized peritonitis	2	
Bronchopneumonia	1	

entered on the third and fourth day of their illness died. For a detailed presentation of the correlation between elapsed time between onset of symptoms and admission and death table 3 is available.

CAUSE OF DEATH

It will be unnecessary to elaborate on the cause of death in the 31 fatal cases, since they are listed in table 4.

It is perhaps fitting to comment that of the 4 deaths listed under the first two groups only 1 was due to intra-abdominal pathologic changes.

CHEMOTHERAPY

Since the publication of the last review, the surgical treatment of appendicitis has been supplemented by chemotherapy. (Penicillin was not used in any case of appendicitis included in this report.) The present medical literature throngs with excellent articles on the use of sulfonamide compounds in abdominal operations. At present the consensus is that intraperitoneal administration of sulfone preparations has a definite and advantageous place in abdominal operations,[15] although there is a tendency to replace it by general administration by other parenteral routes.

It is needless to state that the patients in the earlier cases in this series who were given sulfone compounds did not receive uniform management. Such variations are expected with the advent of a new therapeutic agent. In recent months the management has been standardized to a fair degree. At present, chemotherapy is reserved only for the patients with generalized peritonitis or those in whom its onset is feared. For example, the patients with perforation and abscess formation in whom there is a possibility of extension with resultant generalized peritonitis and those with acute appendicitis without rupture but with contiguous cellulitis, necrosis or possible bacterial perforation are given chemotherapy. At operation (in adult patients) 5 Gm. of sulfanilamide are placed in the peritoneal cavity just before closure. Postoperatively the dose is supplemented by sulfadiazine or its sodium salt in quantities necessary to obtain and maintain a blood level of 8 to 12 mg. per hundred cubic centimeters for as long a period as indicated by the clinical course. Frequent estimates of blood sulfone levels, urinalyses and blood counts help to minimize the possibility of overdosage. Serious complications did not result from the use of sulfonamide drugs. Jaundice was noted in 5 cases, while there was no record of oliguria, anuria, gross hematuria or agranulocytosis. Of 865 patients with acute appendicitis, perforative or nonperforative, 181 received sulfone preparations for the treatment of the primary disease. (Patients who received chemotherapy for complications of appendicitis were not considered.)

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15. (*a*) Waugh, J. M.; McCall, C. H., and Herrell, W. E.: Intraperitoneal Chemotherapy, S. Clin. North America **23**:1144 (Dec.) 1943. (*b*) Intraperitoneal Administration of Sulfanilamide, editorial, J. A. M. A. **119**:796 (July 4) 1942. (*c*) Jackson, A. S.: Chemotherapy in Adjunct to Surgery with Report of Use of Sulfathiazole Intraperitoneally, South. Surgeon **11**:274 (April) 1942. (*d*) Anglem, T. J., and Clute, H. M.: The Intraperitoneal Use of Sulfanilamide in Gastrointestinal Resections, New England J. Med. **229**:432 (Sept. 9) 1943.

In only one group, acute appendicitis with perforation and generalized peritonitis, was the use of sulfonamide compounds of demonstrable value. Of the 167 patients in that group, 114 received sulfonamide drugs, with a mortality rate of 11.3 per cent (13 deaths) as compared with 18.8 per cent (10 deaths) in 53 untreated patients. In 1943 there were no deaths in the class designated perforation and peritonitis, and all the 38 patients had received chemotherapy.

The mortality of the 93 patients with appendicitis and abscess formation was 4.5 per cent and 4.1 per cent respectively for the groups of treated and untreated patients. This difference is too small to be significant. The incidence of postoperative complications and the duration of hospitalization were not grossly influenced by the use of chemotherapy.

SUMMARY

This study shows that there has been a further pronounced reduction of the incidence of acute appendicitis with perforation.

A secondary effect of the decreased incidence of perforation has been the striking rise in the number of cases of acute appendicitis without perforation. That this increase was achieved at the expense of the other groups is evidenced by the fact that it is an absolute increment occurring in spite of a 19 per cent reduction in the total number of cases as compared with that of the previous study.

It would seem important to stress that appendicitis as seen in patients of middle years must be differentiated from conditions which are uncommon in younger patients. Perforation occurred in 58 per cent of the patients with acute appendicitis who were over 40 years.

Since the advent of the educational campaign directed by the Public Health Federation and the Academy of Medicine of Cincinnati, the use of cathartics and the delay in hospitalization have been substantially reduced.

A striking illustration of the successful results of this campaign is drawn from a comparison of our statistics with those of another clinic.

In that study [6a] 1,680 consecutive cases of appendicitis were reviewed. The patients were drawn from a population of 350,000 who lived in an area of 3 square miles (8 sq. km.). The citizens were informed by "various social and medical groups" as to the dangers of catharsis and procrastination with the presence of abdominal pain. There were four hundred and sixteen physicians in this area. Of 1,680 patients, 57.7 per cent were operated on within twenty-four hours after the onset of symptoms and 77.1 per cent within forty-eight hours. Only 41 per cent could be considered charity patients.

In contrast the community of Cincinnati sprawls over 72 square miles (185 sq. km.). The population is 455,610; yet 70.1 per cent of all patients with appendicitis in a 100 per cent charity institution

were hospitalized within forty-eight hours after the onset of symptoms. We anticipate a further improvement in the next review.

In the previous report it was stated that "unless extensive necrosis or actual fecal contamination of the peritoneal cavity is present it is better to close the peritoneum and drain the wound down to it." Our statistics show that this practice may need to be modified. As in the 1934-1938 series, the incidence of postoperative pelvic abscess formation in patients thus treated was significantly greater. There was no striking difference in the mortality rates of patients in whom the wounds were drained to the peritoneum (8.6 per cent) or in whom the peritoneal cavities were drained (12.1 per cent).

There was a further decrease in the mortality rate from appendicitis during the past five years. In a recent paper by Groom,[16] the author noted that "all sections of the country have experienced decreases in appendicitis mortality since 1930. Twenty states had reductions of 60-70 per cent, 20 other states had reductions of 50-60 per cent. The death rate from appendicitis among Metropolitan Life Insurance Industrial Policyholders dropped from 14.4 per 100,000 in 1929 to 5.2 in 1943, a decline of 64 per cent. The resident death rate in Cincinnati (from appendicitis) dropped from 18.4 per cent in 1929 to 4.9 per cent in 1943, a decline of 74 per cent."

In 1929 the death rate from appendicitis in Cincinnati was the second highest of any large city in the country. In the succeeding years intensive effort, for the most part voluntarily and gratuitously given, achieved striking results. "Newspapers, radio, car and bus cards, posters, leaflets, cards and circulars, window exhibits, talks and lectures in schools and at public meetings were employed. Physicians were also bulletined (on the subject) at intervals through the Academy of Medicine." [16] The most convincing testimony as to the effectiveness of this campaign is found in the data submitted by Groom. From its unenviable position as the city with one of the highest death rates from appendicitis in 1929, the city of Cincinnati had the lowest average resident death rate in 1939-1941 from appendicitis of thirteen cities of comparable size chosen at random.

There are some who would attribute the reduced mortality from appendicitis entirely to the sulfone compounds. In our experience chemotherapy has undoubtedly benefited a single group, namely, patients with perforation and peritonitis. An accurate assay of the role played by chemotherapy in the reduction of the death rate from appendicitis is not possible at this time. There are reports [17] that sulfonamide drugs are a major factor in the improvement. We think it only appropriate

16. Groom, W. S.: . A Comparative Study of Mortality 1929-1943 Inclusive—Appendicitis, Public Health Federation of Cincinnati, June 1944.

17. Brett and Watkins.[9] Jackson.[15e]

to emphasize that in this clinic [3] as in others [15a] there has been a steadily decreasing mortality rate from appendicitis which preceded the advent of chemotherapy and that it has not been radically altered by their use.

In the earlier studies sufficient attention was not directed toward certain aspects of appendicitis in the Negro race. A careful study of the statistics indicates that in spite of the imposing results in the educational campaign a certain underprivileged minority has not received the maximum possible benefit from the measures employed. A certain degree of illiteracy, a lower economic status, a lack of telephones and transportation and relatively fewer physicians or interested influential

TABLE 5.—*Comparative Observations on Appendicitis in White and Negro Patients*

	White			Negro		
	Number of Cases		Per Cent of Cases	Number of Cases		Per Cent of Cases
Acute appendicitis; incidence of perforation						
Total number of cases	637			228		
Cases with perforation	173		27.2	87		38.2
Delay in hospitalization for acute appendicitis						
Cases without perforation	461*		26.4	141		30.3
Cases with perforation	173		74.0	86†		81.9
Cathartics in cases of acute appendicitis	Number	Number Taking Cathartics	Per Cent of Total	Number	Number Taking Cathartics	Per Cent of Total
Cases without perforation	464	135	27.2	141	64	45.4
Cases with perforation	173	80	51.4	87	51	58.3
Type of cathartic	Number	Number Taking These Compounds	Per Cent Taking These Compounds	Number	Number Taking These Compounds	Per Cent Taking These Compounds
Magnesium sulfate or castor oil	637	83	14.6	228	71	31.1
Mortality	Total Cases	Deaths	Per Cent of Deaths in Total Cases	Total Cases	Deaths	Per Cent of Total Cases
All appendicitis, including chronic and interval	692	18	59.1	244	13	41.9

* In 3 cases elapsed time not known.
† In 2 cases elapsed time not known.

citizens are factors which well may restrict the efficiency of the campaign described by Groom. The extremely discouraging observations made on appendicitis in the Negro race are listed in table 5. It is found that perforation is 11 per cent commoner in the Negro race. The elapsed time before hospitalization is approximately four to eight hours longer in the groups of cases of acute appendicitis without perforation and with perforation. Among Negroes catharsis is 18.2 per cent more frequent in acute appendicitis and almost 7 per cent commoner in the group in which perforation has occurred. The use of the more violent cathartics (castor oil and magnesium sulfate as examples) is 16.5 per

cent commoner in the Negro race. Finally, the mortality rate in 244 cases of appendicitis in Negro patients was 5.32 per cent (13 of 244 cases) as compared with 2.6 per cent (18 deaths in 692) in white patients. Expressed in another manner, although only 26 per cent of the patients with appendicitis were Negroes 41.9 per cent of the deaths from appendicitis occurred in that race.

CONCLUSIONS

1. The cases of 936 patients with appendicitis who entered the Cincinnati General Hospital in 1939 to 1943 inclusive are reviewed. This article is the third of a series which began with a review of all cases of patients with appendicitis admitted to this institution since 1915 and which will be continued at five year intervals.

2. The incidence of chronic and interval appendicitis was greatly decreased in this five year period. Seventy-one cases, or 7.5 per cent of the total, belong to this group (1934-1938: 232 cases, or 20.1 per cent). This reduction is explained by more stringent criteria imposed on the classification of this group. The incidence of acute appendicitis without perforation showed an absolute and relative increase, 605 cases, or 70 per cent, in comparison to 582 cases, or 63.3 per cent, in 1934-1938. The incidence of perforation in acute appendicitis showed a decrease, 260 cases, or 30 per cent, as against 338 cases, or 36.7 per cent, in 1934-1938.

3. Perforation occurred in 58 per cent of all cases of acute appendicitis in patients over 40 years.

4. Cathartics were employed by 38.3 per cent of all patients with acute appendicitis (1934-1938: 44.5 per cent).

5. The average delay in hospitalization in acute unruptured appendicitis was 26.6 hours, well under the mean of 33.1 hours in 1934-1938. In perforation with acute appendicitis, the average delay in hospitalization was 75.6 hours, almost twenty-five hours less than the mean of one hundred hours in the last study.

6. There has been considerable discussion concerning the operative management of acute appendicitis with perforation. When the two five year periods are combined, analysis shows that the serious complication of pelvic abscess occurred in 33 of a total of 304 patients (10.8 per cent) in whom the peritoneal cavity was drained. This included drains into the pelvis as well as the right paravertebral gutter. On the other hand, there were 21 among 113 patients (18.5 per cent) in whom the peritoneum was closed and only the wound was drained. Thus it is seen that the frequency of this complication was greater when the peritoneal cavity was not drained. However, in this ten year period it is only fair to point out that in these same two groups the mortality

rate was 13.8 per cent with intra-abdominal drainage and 8.8 per cent with drainage of the wound alone. However, it should be stressed that the patients with peritoneal drainage were usually much sicker at the onset than those without peritoneal drainage and also that there were 304 cases in the former group and only 113 cases in the latter group.

7. The reduction in mortality from appendicitis may be attributed at least in part to an intensive educational campaign begun in 1934, at which time Cincinnati's death rate from appendicitis was among the highest of those in large cities in the United States. A recent survey demonstrates Cincinnati's mortality rate from appendicitis in 1943 to be among the lowest of those in thirteen cities of comparable size and racial composition.

8. The exact role of sulfone therapy in the reduced mortality rate cannot be determined at this time, because of insufficient data. Chemotherapy seemed to be of assistance in the group of cases classed acute appendicitis with perforation (mortality 13.77 per cent against 17.22 per cent in 1934-1938). The next survey from this clinic will be based on sufficient data to enable a more comprehensive estimate of the value of sulfonamide therapy.

9. Appendicitis as seen in the Negro race is a disease of severer proportions than that in the white race. The mortality rate is 5.3 per cent as against 2.6 per cent among white patients. Deaths among Negro patients (13) composed 41.9 per cent of the deaths for the entire series. Should the educational campaign be more effectively focused on this group, a significant improvement in the morbidity and mortality rate of appendicitis in the Negro race may be expected.

TREATMENT OF POISONING WITH RATTLESNAKE VENOM

Experiments with Negative Pressure, Tourniquet and Bulb Suction

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DURING the first decade of this century the use of serums (antivenin) in the treatment of snake bite became widespread, and investigation of other methods came almost to a standstill. Limited effectiveness, high cost and allergy to large quantities of horse protein are serious handicaps to the use of serum. For this reason the continued investigation of other therapeutic measures, such as mechanical extraction of venom by various types of suction, is highly advisable.

Experiments by Dr. Dudley Jackson [1] and co-workers have proved that venom of the Texas diamond-backed rattlesnake (Crotalus atrox) can be removed locally for many hours after injection of the venom by restricting absorption with a tourniquet and applying suction to cruciate incisions made in the neighborhood of the bite.

In perusing papers by Jackson and others, we became interested in the possibility of developing a better method for extracting venom by suction and also in determining just what part of Jackson's results could be attributed to constriction by the tourniquet and what part to suction. A study of the literature failed to reveal any reports on the use of a tourniquet alone except in Australia, where Fairley [2] got only negative results in working with the effects of elapid venom on sheep. Even when he used Russell's viper (Vipera russelii) venom in relatively small amounts (less than two minimum lethal doses) his results were largely negative.

We designed our experiments to test the relative efficacy of three forms of local therapy, used individually and in combination: (1) nega-

These experiments were performed in the Department of Surgery, University of Illinois College of Medicine. Dr. Warren H. Cole, Head of the Department of Surgery, gave many helpful suggestions. Valuable technical assistance was rendered by Mr. Everett Hoppe and Mr. Wilmer Eigsti.

1. (*a*) Jackson, D.: First Aid Treatment for Snake Bite, Texas State J. Med. **23**:203, 1927. (*b*) Jackson, D., and Harrison, W. T.: Mechanical Treatment of Experimental Rattlesnake Venom Poisoning, J. A. M. A. **90**:1928 (June 16) 1928. (*c*) Jackson, D., and Githens, T. S.: Treatment of Crotalus Atrox Venom Poisoning in Dogs, Bull. Antiven. Inst. America **5**:1, 1931.

2. Fairley, N. H.: Criteria for Determining the Efficacy of Ligature in Snake Bite, M. J. Australia **1**:377, 1929.

tive pressure, (2) the tourniquet and (3) suction as applied by Jackson. The first of these is new.

EXPERIMENTAL METHODS

All the venom used in our experiments had been milked from Texas diamond-backed rattlesnakes (Crotalus atrox) at Ross Allen's Reptile Institute, Ocala, Fla. The venom, received in desiccated form, was prepared for use by dissolving the desired amount in from 1 to 2 cc. of distilled water. The dogs were anesthetized with intraperitoneal injections of 3 per cent pentobarbital sodium in the dose of 0.5 cc. per pound (0.5 Kg.) of body weight. We used the previously calculated [1a]

TABLE 1.—*Treatment by Alternating Negative Pressure*

Negative Pressure (mm. Hg) and Duration, Minutes	Number of Minimum Lethal Doses Injected	Weight of Dog, Lb.	Type and Number of Incisions; Interval Before Incisions	Amount of Fluid Extracted, Cc.	Results
120 for 10 400 for 10 120 for 15 60 for 5	3	22	Cruciate incision at site of injection and ring-cut above 15 min. after injection *	130	Survived
120 for 10 60 for 10 Alternately for 1 hour	8	22	Cruciate incision at site of injection 30 min. after injection †	120	Survived
120 for 10 60 for 10 Alternately for 1 hour	8	15	Cruciate incision at site of injection 35 min. after injection *	85	Survived
120 for 10 60 for 5 Alternately for 1 hour	8	47	Cruciate incision at site of injection 30 min. after injection *	233	Survived
120 for 8 60 for 2 Alternately for 1 hour	8	19	Incision made at site of injection 30 min. after injection *	155	Died in 42 hr.
120 for 8 60 for 2 Alternately for 1½ hours	8	12	Cruciate incision at site of injection 30 min. after injection; 2 more made 1 hr. after first *	82	Died in 24 to 48 hr.
120 for 8 60 for 2 Alternately for 1½ hours	8	15	5 puncture-like cruciate incisions made 20 min. after injection; 2 more made 1 hr. after the 5th ‡	50	Died in 24 hr.

* Negative pressure applied immediately after incision.
† Negative pressure not applied until 20 minutes after incision because of difficulty in arresting excessive bleeding.
‡ Negative pressure not applied until 10 minutes after incision.

minimum lethal dose of venom for dogs, which is 1 mg. of desiccated venom for every pound (0.5 Kg.) of the dog's weight. The venom was always injected subcutaneously on the outside of the dog's hindleg, about halfway between the ankle and the knee.

Using 9 dogs, Jackson established the minimum lethal dose of venom injected subcutaneously as 1 mg. for each pound of body weight. All the dogs died in five days. We checked this minimum lethal dose with 7 dogs, of which 2 died in twenty-four hours, 1 in forty-eight and 1 in seventy-two. Three other dogs given injections of two, three and eight minimum lethal doses died in seventy, twenty-two and twenty-three hours respectively.

A. Negative Pressure Experiments.—The apparatus necessary for the experiment was a large-mouthed glass bottle with a screw top. An oval opening in this metal top was surrounded by a metal cuff into which a dog's leg would fit snugly. Petrolatum and a strip of rubber dam served to make a moderately airtight connection between leg and cuff. There were two connections to the apparatus, one through which the negative pressure was applied by a suction pump and the other for measurement of the pressure with a manometer. A calculated amount of snake venom was injected into the dog's leg and, after half an hour, several cruciate (1 cm.) incisions were made through the skin of the area previously receiving the snake venom and the limb inserted into the suction bottle. This apparatus would probably be available only at hospitals, and it would take the patient at least thirty minutes to get to the nearest hospital. Therefore, thirty

TABLE 2.—*Treatment by Tourniquet*

Number of Cases	Number of Minimum Lethal Doses Given Each Dog	Weight of Dog, Pounds	Interval Before Applying Tourniquet, Minutes	Duration of Constriction, Hours	Results: Survived Injection, Hours§
1	4	24	None	23	144
1	4	25	None	8-18	144
2	4	17, 22	3-5	17½	162
1	4	17	3-5	17½	138
1	4	21	3-5	17½	18 *
2	6	18, 24	None	6	144
2	6	10, 18	1	17	137
1	6	11	1	16½	89
1	6	12	1	17	17 †
1	8	13	None	4	144
2	8	10, 14	None	5, 6	23
1	8	13	None	5¾ ‡	23
1	8	19	None	5½ ‡	72
1	8	15	None	5¾ ‡	120
3	8	16, 21, 24	5	19	162
1	8	12	1	18	168
1	8	12	1	18	114
1	8	13	1	18	90
1	8	7	1	18	42
1	8	26	5	19	19

* Dog probably died from combined effects of venom and distemper.
† Dog sensitive to pentobarbital sodium; probably died from combined effects of venom and pentobarbital sodium.
‡ Tourniquet pressure alternated between 120 mm. Hg for nine minutes and 60 mm. Hg for one minute during the first 1½ hours of treatment.
§ Many of these dogs were killed because of serious secondary infection.

minutes was allowed to elapse before application of negative pressure, which was then exerted on the leg for a period of one hour, alternating between 60 and 120 mm. of mercury. Variations were made as to time and pressure on the 7 dogs, as set forth in table 1.

B. Tourniquet Experiments.—To evaluate the benefit obtained from the various parts of Jackson's combined therapy,[1] we devised a group of experiments using only the tourniquet. After the venom had been injected into the anesthetized dog the tourniquet was applied proximal to the site of injection. It was not placed tightly enough to interrupt arterial flow but merely to obstruct venous and lymphatic return, and it was left in place from four to twenty-three hours. The procedure was carried out on a total of 26 dogs, as shown in table 2. Little or no time was allowed to elapse after injection of the venom, because we felt that this type of treatment would be available without loss of time to any person exposed to snake bites.

C. Suction Experiments.—Our third group of experiments was designed to test the efficacy of suction (as applied by cupping) to numerous 1 cm. cruciate incisions over the site of injection of venom. This form of therapy was applied to 4 dogs receiving injections of three, four and eight minimum lethal doses of snake venom, as shown in table 3.

D. Tourniquet and Suction Experiments.—The fourth type of experiment was performed on only 2 dogs. On these we combined the tourniquet with suction by cupping, as shown in table 4.

TABLE 3.—*Treatment by Bulb Suction (Without Tourniquet)*

Number of Minimum Lethal Doses Injected	Weight of Dog, Lb.	Type and Number of Incisions; Interval Before Incisions	Type and Duration of Suction; Interval Before Application of Tourniquet	Results
3	18	Cruciate incision at site of injection made at once; 4 additional incisions made later	Suction begun at once after making first cut, and continued 4 hr.; 2 bulbs used alternately on multiple cuts	Survived
4	12	Cruciate incision at site of injection made at once; 4 additional incisions made later	Suction begun at once after making first cut, and continued 4 hr.; 2 bulbs used alternately on multiple cuts	Survived
8	18	Cruciate incision at site of injection made 5 minutes after injection; 6 additional incisions made later	Suction begun at once after making first cut, and continued 2 hr.; 3 bulbs used alternately on multiple cuts	Died in less than 24 hours
8	21	Cruciate incision at site of injection made 5 minutes after injection; 2 additional incisions made later	Suction begun at once after making first cut, and continued 2 hr.; bulbs used alternately on multiple cuts	Died in less than 24 hours

TABLE 4.—*Treatment by Tourniquet and Bulb Suction*

Number of Minimum Lethal Doses Injected	Weight of Dog, Lb.	Type and Number of Incisions; Interval Before Incisions	Type and Duration of Ligation	Type of Suction	Results
8	14	Cruciate incision at site of injection made 30 min. after injection	Tourniquet applied for 1 hr. at 120 mm. Hg for 10 min. and then 60 mm. for 10 min.	Single bulb used 1 hr.	Died within 72 hr.
8	32	Cruciate incision at site of injection made 30 min. after injection	Pressure of tourniquet alternated for 1 hr. between 120 mm. Hg for 9 min. and 60 mm. for 1 min.	Single bulb used 1 hr.	Survived

RESULTS OF EXPERIMENTS

A. Negative Pressure.—The first 4 dogs subjected to the negative pressure treatment, with the affected limb in a suction bottle as described, survived. Three of these dogs had been given injections of eight and the fourth of three minimum lethal doses of venom. Three additional dogs (receiving eight minimum lethal doses) died in spite of therapy; their survival time was no longer than that in the control animals. The

mortality rate of dogs receiving eight minimum lethal doses of venom and subjected to this form of treatment was therefore 50 per cent, as shown in table 1.

B. The Tourniquet.—Table 2 gives the details and results of twenty-six experiments in which the tourniquet was the only form of therapy. Nineteen of the dogs given injections of four, six or eight minimum lethal doses of venom survived seventy-two hours or more. Survival for this length of time was interpreted as protection against the venom; it was necessary to kill many of these animals at the time because of secondary infection which developed in the ulcers produced by the local necrotizing effect of the venom. By this form of treatment, the mortality was reduced to 17 per cent when four and six minimum lethal doses of venom were injected and to 36 per cent when eight minimum lethal doses were given.

C. Suction.—Having investigated the effects of constriction by tourniquet, we felt it imperative to determine the value of suction alone. Jackson has already reported ten suction experiments with successful results on dogs that had received one to four and a half minimum lethal doses of Crotalus atrox venom. Our 2 dogs given injections of three and four minimum lethal doses survived with this form of therapy, whereas the 2 receiving eight minimum lethal doses died.

D. Tourniquet and Suction.—With the efficacy of the tourniquet and the suction treatment proved, it is reasonable to assume that the combination of the two would be better than either alone. Only 2 dogs were used in this group of experiments; 1 of them died from effects of the venom, as shown in table 4.

SUMMARY AND CONCLUSIONS

The survival of 4 out of 7 dogs treated by alternating negative pressure is evidence that the negative pressure method has possibilities; it would appear to be the most effective way to extract the venom. Impracticality is the chief drawback to this method. This drawback is not so serious if the method proves to be appreciably better than others that also call for hospital treatment. Rubber or glass boots (Pavex boot) for the application of alternating and negative pressure are standard equipment in many hospitals and can be adapted for this treatment. Further investigations of negative pressure are indicated.

The tourniquet experiments prove beyond doubt that moderately tight constriction above the site of injection of the venom greatly prolongs life and may even save it by slowing down the absorption of venom. Although the venom starts immediately to diffuse through the tissues and eventually travels up the lymphatic vessels to enter the systemic circulation, absorption is greatly retarded by the tourniquet.

Since the saving of life is probably accomplished at the cost of intensifying the local effects, constriction by tourniquet must be placed primarily in the category of first aid treatment. When competent medical aid is reached, the physician in charge will have to decide about continued use of the tourniquet.

Mild suction applied to cruciate incisions made over and through the site of injection of the venom extracts blood and serum that contain a high concentration of venom. This has been proved by injecting the exudate into another dog. Any venom extracted makes that much less for the body to detoxify and of course may mean the difference between life and death. Although suction has less practical value than has application of a tourniquet there are a limited number of bites on the head, neck and trunk that cannot be treated with a tourniquet.

In this group of experiments, the efficacy of antivenin was not tested, but there is evidence in other reports suggesting that it is by no means completely effective.

Our experiments supply additional evidence that application of a tourniquet (applied tightly enough to constrict flow of lymph and venous blood but not arterial), followed by mild suction over small cruciate incisions at the site of the snake bite, is an effective form of therapy, even when the quantity of venom is as great as eight minimum lethal doses.

COMPARATIVE EFFICACY OF BLOOD FROM NORMAL AND FROM BURNED DONORS IN EXPERIMENTAL BURNS

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AND
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With the Technical Assistance of Joan W. Zerbe, B.A.

EFFORTS to explain the clinical course of patients receiving extensive superficial burns have led many clinicians to postulate the presence of a circulating toxin. Most of the experimental evidence presented in support of this view has been subject to the criticism that the treatment accorded the material removed from the burned animal might have contributed to its effect on the recipient. Since a simple transfusion of blood from a burned animal to a normal animal is generally well tolerated by the latter, it was decided to increase the possible sensitivity of the recipient to a hypothetic toxin by subjecting it, under ether anesthesia, to a standardized burn prior to the transfusion. The burn had been shown to result in a mortality of approximately 50 per cent in untreated animals. A second series of controls was employed, which was given transfusions of equivalent amounts of blood from normal animals.

METHODS

Wistar rats were used as the test animals. All animals received a back burn of 32 per cent ± 2 of their total body surface by immersion in a water bath maintained at 90 C. ± 0.25 for fifteen seconds. The details of the method have been reported by McCarthy.[1]

For most experiments 12 stock rats, 6 weighing between 190 and 200 Gm. and 6 weighing between 200 and 210 Gm., were selected at random from stock cages. These again, by random selection, were divided into three groups of 4 in such a way that every group contained 2 animals in each weight range. After the burn, one group was infused with whole blood from burned rats, according to a method which will be described in detail later. Such blood is referred to in this paper as "postburn blood." One of the two remaining groups of 4 was infused with whole normal blood, and the third group served as the untreated controls.

The infusions of postburn and normal blood were in amounts based on 2 per cent of the body weight of the animals to be infused. They were given in all

From the Harrison Department of Surgical Research, University of Pennsylvania Schools of Medicine.

1. McCarthy, M. D.: A Standardized Back Burn Procedure for the White Rat Suitable for the Study of the Effects of Therapeutic and Toxic Agents on Long Term Survival, J. Lab. & Clin. Med. **30**:1027, 1945.

cases two hours following the burn and at the rate of 1.0 cc. per minute. The unanesthetized rats were tied on their backs to a restraining board. The infusions were given into the internal saphenous vein through a small incision in the skin. After the infusion the vein was compressed at the point of the needle puncture by a sterile sponge and then ligated above and below the site of puncture. Sterile topical thrombin was dusted into the cutaneous incision, which was then closed by two interrupted sutures. This procedure was found necessary to prevent bleeding from the site of injection and from severed capillaries of the skin due to the heparin content of the infused blood.

PREPARATION OF POSTBURN AND NORMAL BLOOD FOR INFUSION

Four hours after the burn the hematocrit values for rats receiving a burn of 45 per cent of the total body surface were about 140 per cent of the initial level. The viscosity of the blood from burned animals was such that it could be infused through a no. 27 gage needle only with great difficulty. To facilitate infusion and to obtain a cell-plasma ratio equivalent to that of the normal, the hematocrit level of the postburn blood was adjusted to 50 per cent by the addition of postburn plasma.

Postburn plasma was obtained by burning 4 large rats (300 to 400 Gm.) on the day preceding infusion. A 45 per cent $\pm$ 2 burn of the body surface produced an injury which invariably resulted in death within twenty-four hours. Four hours after the burn these animals were given 100 Toronto units of heparin (Connaught Laboratories) intravenously. Immediately thereafter, blood was withdrawn, by cardiac puncture, into a sterile 10.0 cc. syringe which had been wet with heparin solution. Approximately 3.0 cc. of blood was withdrawn from each rat; all samples were pooled in a 15.0 cc. graduated sterile centrifuge tube.

The same procedure being followed, blood was obtained from normal unburned animals and likewise pooled in a 15.0 cc. sterile centrifuge tube. Both postburn and normal blood were centrifuged for one-half hour at 2,500 rotations per minute. Great care was taken in removing the plasma to avoid contamination by the components that make up the buffy coat. The postburn plasma and the normal plasma thus prepared were placed in the freezing unit of an electric refrigerator in sterile containers and frozen.

Whole postburn blood and whole blood from normal animals were obtained in the same manner approximately sixteen hours before infusion and stored at 5 C.

On the day of the experiment the whole blood and plasma were brought to room temperature and then centrifuged for thirty minutes at 2,500 rotations per minute. A sufficient volume of stored postburn

plasma was then added to the whole postburn blood to give a 50 per cent hematocrit value.

In order to eliminate storage of part of the postburn plasma as an uncontrolled factor in the experiment, the normal whole blood was prepared by substitution of a like amount of stored normal plasma in it before it was infused. That is, after whole blood was drawn from normal animals, sixteen hours before the experiment, enough of the plasma was drawn off to raise the hematocrit level to that of the postburn blood. Stored normal plasma was then added to adjust the hematocrit level to 50.

RESULTS

A total of 48 rats was used in the experiments, of which 16 rats each received a single infusion of 2 per cent of its body weight of whole

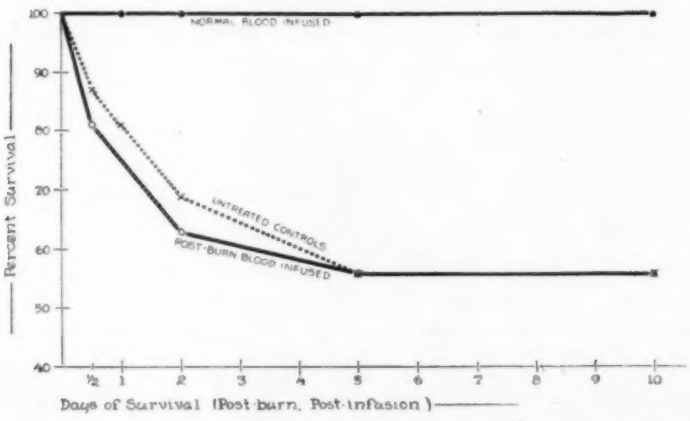

Chart 1.—The effect on survival of burned rats infused with normal and postburn blood.

postburn blood, 16 rats each received a single infusion of 2 per cent of its body weight of whole normal blood and 16 rats received no infusion.

Chart 1 shows the survival percentages of the three groups for a ten day period. A 56 per cent survival was obtained in the untreated group, and a 56 per cent survival occurred in the group receiving the postburn blood infusion. A 100 per cent survival was obtained in the group infused with normal whole blood. The survival of the normal blood group compared with that of the postburn blood and untreated control groups shows a highly significant difference on statistical analysis.

Hematocrit values expressed in per cent of the hematocrit value obtained before the burn are recorded in chart 2. The data are not well correlated with the survival rates of the different groups.

In view of the recent work of Tabor and Rosenthal,[2] which demonstrated a pronounced increased sensitivity to potassium changes in shocked animals, plasma potassium levels were determined on several samples of both normal and postburn blood prepared according to the technic described.

The Charnock and Montgomery method [3] being used, the average potassium level of the postburn plasma was 33.1 mg. per hundred cubic centimeters and that of the normal plasma was 30.5 mg. per hundred cubic centimeters. The increase of approximately 3.0 mg. per hundred cubic centimeters of potassium in the postburn plasma over that in the normal plasma, judging from Tabor and Rosenthal's [2] data, would hardly be sufficient in itself to explain the difference in survival between the two infusion groups. Hemoglobinemia was measured on the same

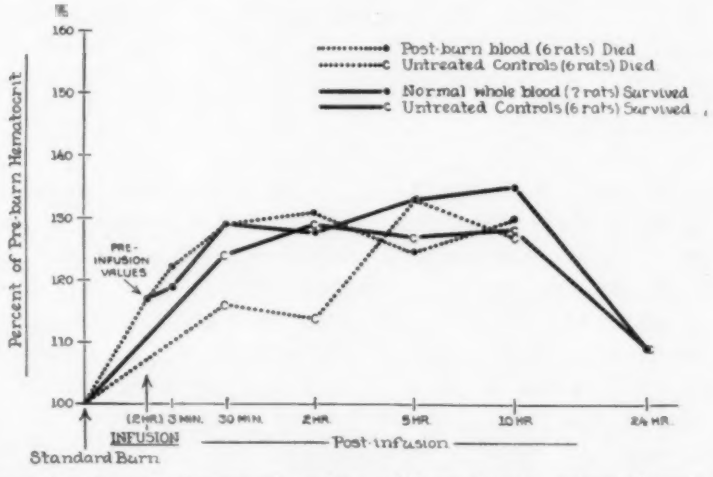

Chart 2.—Average hematocrit values of burned rats untreated and infused with normal and postburn whole blood.

samples by the spectrophotometric method. An average value of 75.0 mg. per hundred cubic centimeters was found in the normal plasma and an average of 407.0 mg. per hundred cubic centimeters in the postburn plasma.

In an effort to determine which of the constituents of the whole postburn blood was responsible for the decreased survival reported, a cellular suspension of cells from burned rats was prepared in isotonic solution of sodium chloride. These cells were obtained from postburn blood prepared as previously described. To the postburn cells was

2. Tabor, H., and Rosenthal, S. M.: Experimental Chemotherapy of Burns and Shock: VIII. Effects of Potassium Administration, of Sodium Loss and Fluid Loss in Tourniquet Shock, Pub. Health Rep. **60**:373, 1945.

3. Charnock, F. W., and Montgomery, E. H.: Unpublished data.

added an equal volume of isotonic solution of sodium chloride. A similar suspension of normal red cells was simultaneously prepared. Twenty-four animals receiving the standardized 32 per cent burn described were infused with these two suspensions of red cells. Twelve animals received postburn cells in isotonic solution of sodium chloride, and 12 animals received normal cells in isotonic solution of sodium chloride. Eight of the 12 animals (66 per cent) which received the postburn cells survived, whereas 10 of the 12 animals (83 per cent) which received normal cells survived. There is no significant statistical difference in survival between these two groups, but both showed an increased survival over that of the untreated controls, which was 56 per cent. No significant differences in hematocrit values were observed between these two infusion groups or between the survivors or dead animals of either group. These results suggest that the changes induced in the blood of burned donors are likely to be found in the plasma. Further studies on the chemical alterations of postburn plasma are in progress.

COMMENT

Prior to the experiments reported here in detail we had confirmed the fact that a single transfusion of blood from a burned rat was not lethal to a normal rat in amounts up to 2 per cent of the body weight. It was felt that any attempt to extract or concentrate a toxic factor in the postburn blood might result in the production of new substances or in the concentration of normal constituents, such as potassium, in amounts which would be toxic. Therefore, the other alternative, of increasing the sensitivity of the test animal by producing a burn which yielded a standard mortality rate, was selected. The usefulness of this method depended on whether or not it would be possible to standardize a burn accurately enough to predict the mortality. The method evolved for this has been published by one of us (M. McC.), and, while it is affected to some extent by seasonal factors, we believe that it is reliable when controls are run simultaneously.

For several decades the possibility that thermal burns produce a toxic material which is distributed widely in body fluids has been considered. In 1923 Robertson and Boyd [4] reported experiments which seemed to support such a view. Their conclusions were questioned by Underhill and Kapsinow,[5] and by 1930 the interest of most investigators in this field was focused on the part played by the fluid and

4. Robertson, B., and Boyd, G.: Toxemia of Severe Superficial Burns in Children, Am. J. Dis. Child. **25**:163 (Feb.) 1923.

5. Underhill, F. P., and Kapsinow, R.: The Alleged Toxin of Burned Skin, J. Lab. & Clin. Med. **16**: 823, 1931.

electrolyte shift in the burned patient. Underhill and his associates [6] have attributed all or most of the systemic disturbances of burns in the first few days following the burn to a combination of fluid and salt depletion of the blood. However, in 1937 Wilson, Jeffrey, Roxburgh and Stewart [7] reported that the protein-containing fraction in the bleb fluid of secondary burns was toxic to animals, especially if it was not collected at once but after forty-eight hours.

In 1940 Wolff, Elkinton and Rhoads [8] noted changes in hepatic function and glucose tolerance in burned patients in whom shock had been prevented by prompt treatment with plasma. Unfortunately, their patients were treated locally with tanning agents which were later shown to be capable of producing hepatic injury in animals and in human beings.[9]

The experiments of Netsky and Leiter, in 1943,[10] in which an increase in capillary permeability for horse protein occurred in the dog ten minutes after the burn, are of especial interest. They showed not only an increased rate of appearance of the horse protein in the lymph from the burned area but also an increase in the lymph from the unburned area. This seemed difficult to explain, unless an injurious substance was circulating in the blood, a substance essential for normal capillary permeability was withdrawn from the blood or a change in capillary permeability was brought about by nerve control. It was not thought that there was a widespread anoxia at the time the change was first observed.

In the experiments reported here the transfusion of postburn blood did not increase the mortality as compared with that of untreated controls. It did, however, result in a significantly higher mortality than was observed in the animals receiving equal amounts of normal blood. This could be interpreted as indicating the presence of small amounts

6. Underhill, F. P.; Fisk, M. E., and Kapsinow, R.: The Extent of Edema Fluid Formation Induced by a Superficial Burn, Am. J. Physiol. **95**:325, 1930. Underhill, F. P., and Fisk, M. E.: The Composition of Edema Fluid Resulting from a Superficial Burn, ibid. **95**:330, 1930. Underhill, F. P.; Fisk, M. E., and Kapsinow, R.: The Relationship of the Blood Chlorides to the Chlorides of Edema Fluid Produced by a Superficial Burn, ibid. **95**:334, 1930.

7. Wilson, W. C.; Jeffrey, J. S.; Roxburgh, A. N., and Stewart, C. P.: Toxin Formation in Burned Tissues, Brit. J. Surg. **24**:601, 1937.

8. Wolff, W. A.; Elkinton, T. R., and Rhoads, J. E.: Liver Damage and Dextrose Tolerance in Severe Burns, Ann. Surg. **112**:159, 1940.

9. Saltonstall, H.; Walker, J.; Rhoads, J. E., and Lee, W. E.: The Influence of Local Treatment of Burns on Liver Function, Ann. Surg. **121**:201, 1945.

10. Netsky, M. G., and Leiter, S. S.: Capillary Permeability to Horse Proteins in Burn-Shock, Am. J. Physiol. **140**:1, 1943.

of an injurious factor, which counteracted the beneficial effects of the transfusion, or possibly as indicating deficiency of the properties which made the normal blood effective.

SUMMARY

Rats subjected to a standardized scald burn were infused with postburn whole blood and normal whole blood. The survival rates of these animals were compared with those of simultaneous untreated controls. The group infused with the postburn blood showed a survival rate similar to that of the untreated group. The animals infused with the normal blood showed a significantly higher survival rate than either of the other two groups. Hematocrit data were obtained from all groups. These give no indication that increased mortality is a direct result of increased hemoconcentration. Suspensions of postburn and normal cells in isotonic solution of sodium chloride were tested. Both promoted increased survival in the test animals when compared with untreated animals; however, the difference between them was not statistically significant. The plasma potassium levels were slightly higher in the postburn blood than in the normal blood. Hemoglobinemia was found to increase from an average value of 75.0 mg. per hundred cubic centimeters in the normal plasma to an average value of 407.0 mg. per hundred cubic centimeters in the postburn plasma.

CONCLUSION

Blood from burned rats was ineffective in treatment of rats subjected to a standardized thermal burn resulting in a 44 per cent mortality rate in the untreated controls.

The difference between the mortality rate resulting after transfusion with blood from burned rats (44 per cent) and the mortality rate resulting after transfusion with normal blood (0 per cent) is statistically significant.

Dr. J. E. Rhoads and Dr. Harry M. Vars gave helpful suggestions and criticisms during the course of experimentation and preparation of the manuscript.

BURN SHOCK

Its Treatment with Continuous Hypodermoclysis of Isotonic Solution of Sodium Chloride Into the Burned Areas; Clinical Studies in Two Cases

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AND
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IN A PREVIOUS paper,[1] one of us (J. K. B.) reported the results of experimental studies on burn shock when treated with isotonic solution of sodium chloride injected by hypodermoclysis into the burned area. These studies revealed the following significant facts: 1. There is a loss of water and electrolytes, chiefly salt, followed by plasma proteins into the burned area. 2. This loss continues until pressure in the tissue spaces equals the hydrostatic pressure within the capillaries. Then reabsorption begins but in the reverse manner. That is, colloids are returned first by the lymphatic vessels, which behave as a semipermeable membrane. Then crystalloids are absorbed by the capillaries. 3. The loss of plasma occurs earlier in the more severely (third degree) than in the less severely burned animals. 4. Treatment by hypodermoclysis of isotonic solution of sodium chloride into the burned area seems to decrease the amount of water and plasma lost, and it facilitates the absorption of both. 5. It is thus an autotransfusion of lost colloids and crystalloids and, in addition, is a method for supplying quickly the great demand for salt by injured tissues. 6. It makes possible the dilution and excretion of hypothetic toxins, helps control body temperature and prevents pulmonary edema and anuria. 7. Human skin is not as loosely attached to the subcutaneous tissue as is that of the dog, and therefore multiple injections would be necessary, but much less solution would be needed to produce an intercellular hydrostatic pressure above that of effective capillary pressure.

Recently this method of treatment was used in 2 patients who were burned so extensively that their conditions seemed hopeless. Their burns were due to an explosion of a large tank filled with steaming hot sodium hydroxide. The solution was so strong that practically all the clothes worn by the men fell off their bodies in shreds.

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1. Berman, J. K.; Peterson, L., and Butler, J.: The Treatment of Burn Shock with Continuous Hypodermoclysis of Physiological Saline Solution into the Burned Area, Surg., Gynec. & Obst. **78**:337-345 (April) 1944.

One plasma transfusion (500 cc.) was given to each of the men. Transfusions of whole blood were used at strategic intervals. Although 1 patient (J. E. M.) died after forty days, the other (M. H. P.) survived and is well. In both cases burn shock was controlled or prevented almost entirely by continuous hypodermoclysis of isotonic solution of sodium chloride.

REPORT OF CASES

CASE 1.—J. E. M., a 41 year old white man was admitted to the Methodist Hospital at Indianapolis at 5 p. m. on Feb. 16, 1946. About thirty minutes before admission he was burned by hot sodium hydroxide, the result of an explosion of a large tank containing the solution. The burns proved to be second and third degree and involved about 72 per cent of the body surface. The extent of the burned area was estimated by the Berkow [2] and Lund-Browder [3] methods, and the burns were distributed as follows: head, 3 per cent; neck, 1 per cent; anterior part of the trunk, 0 per cent; posterior part of the trunk, 13 per cent; buttocks, 5 per cent; genitalia, 1 per cent; upper part of the arms, 6 per cent; forearms, 6 per cent; hands, 4.5 per cent; thighs, 17 per cent; legs, 13 per cent, and feet, 3 per cent. The total equals 72.5 per cent (fig. 1).

The patient did not appear to be in shock. He was alert and apprehensive and complained of severe pain and coldness. His pulse rate was 130, regular and weak; the respiratory rate was 30, and respirations were shallow, with some dyspnea and an expiratory grunt. Oral temperature was 99 F. The blood pressure was not obtained because both arms and legs were burned. Moist rales could be heard anteriorly in the lower fields of both lungs.

Prior to admission the man was given ¼ grain (0.016 Gm.) of morphine sulfate subcutaneously and 500 cc. of citrated plasma intravenously. Laboratory studies on admission gave the following results: hematocrit reading, 56.5 volumes per cent; plasma protein content, 7.2 Gm.; hemoglobin content, 18 Gm.; erythrocyte count, 5,500,000, and leukocyte count, 27,500, with 95 per cent polymorphonuclears; urinalysis showed specific gravity of 1.038; the albumin content was 2 Gm. per hundred cubic centimeters and sugar content 1.8 Gm. per hundred cubic centimeters.[4]

Treatment.—The patient was given ¼ grain (0.016 Gm.) of morphine sulfate intravenously. Sterile, dry gauze dressings were loosely applied to the extremities,

2. Berkow, S. G.: Method of Estimating Extensiveness of Lesions (Burns and Scalds) Based on Surface Area Proportions, Arch. Surg. **8**:138-148 (Jan., pt. 1) 1924.

3. Lund, C. C., and Browder, N. C.: The Estimation of Areas of Burns, Surg., Gynec. & Obst. **79**:352-358 (Oct.) 1944.

4. Laboratory methods: Hematocrit and plasma protein levels were determined by the copper sulfate method for measuring specific gravities (Phillip-Van Slyke and associates); albumin-globulin contents by Kingsley's method for use in Howe's micro-Kjeldahl test; the urine albumin content (quantitative) by Purdy's method; blood sugar levels by the Folin-Wu method; urine sugar (quantitative) by Gerrard-Allen's method; nonprotein nitrogen levels by the Folin-Wu method; carbon dioxide–combining power by Van Slyke's method; blood chloride contents by the "Whitehorn" modification of Volhard's method, and blood calcium levels by Clark-Colly's modification of the Kramer-Tisdall method.

without any attempts to cleanse or antiseptize the wounds. A large 4 ply sterile gauze pad was placed on the bed for the patient to be on, and a cradle was used to keep the sheets and blankets off the burns. No heat was employed externally.

Isotonic solution of sodium chloride was injected by hypodermoclysis into the burned areas by continuous drip. This was accomplished by use of ordinary 1,000 cc. flasks of sterile isotonic solution of sodium chloride equipped with Y tubes and 20 gage, 4 inch (10 cm.) needles. The needles were moved to various parts of the body, all burned areas being kept distended. The infusions were used continuously for ninety-six hours in the amount of 3,000 to 4,000 cc. in twenty-

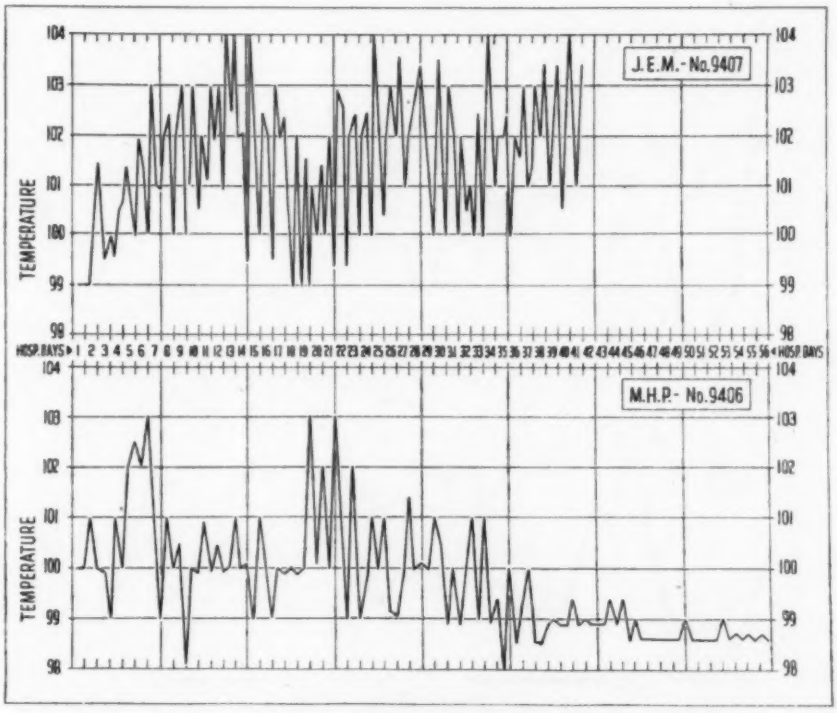

Fig. 1.—The oral temperature (Fahrenheit). Note that J. E. M. had a remittent fever, with temperature up to 104 F. for seventeen days. At this time his temperature tended toward the intermittent type, and its peaks were up to 103 F. Note that at this time the leukocyte count was 15,000, with 84 per cent polymorphonuclears; the fluid intake, 3.5 liters; the urinary output, 2 liters, with specific gravity of 1.015 and no blood in the urine; hemoglobin content, 12.3 Gm.; red blood cells, 4,000,000; hematocrit reading, 45 volumes per cent, and plasma protein level, 4.2 Gm. After this apparent improvement, the patient became worse and the temperature again reached 104 F. and did not at any time fall below 100 F., despite cold sponges on the face, neck and chest carried out by continuous nursing care.

M. H. P. also had a turning point, which occurred on the nineteenth day, with temperature up to 103 F.; leukocyte count, 10,000, with 88 per cent polymorphonuclears; fluid intake, 4.5 liters; urinary output, 4 liters, with specific gravity of 1.012 and no blood in the urine; hemoglobin content, 12.3 Gm.; red blood cells, 4,000,000; hematocrit reading, 41 volumes per cent, and plasma protein content, 4.6 Gm. The patient was in a coma.

four hours. In addition, enteric-coated, 5 grain (0.32 Gm.) sodium chloride tablets were given by mouth; these produced nausea and vomiting, and the administration of them was discontinued after the first day. Penicillin, 30,000 units, was injected intramuscularly every three hours. Tetanus antitoxin, 1,500 units, was given subcutaneously.

A bland, high protein diet was ordered. This included beef broth, beef, cottage cheese, gelatin, milk, buttermilk, custard, bread, potatoes, macaroni and cheese and other foods requested by the patient. Water, tea and sweetened drinks were given as desired, the total calories being about 5,000. Morphine, ¼ grain (0.016 Gm.) was used to relieve pain. Enemas of isotonic solution of sodium chloride were given as needed. A cannula was inserted into the right antecubital vein, and 500 cc. of citrated whole blood was given each day for the first three days.

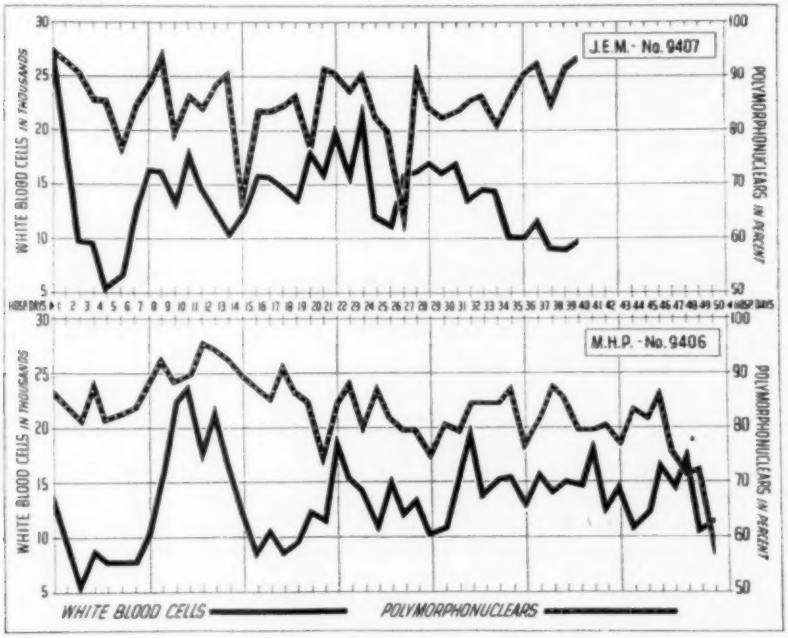

Fig. 2.—Leukocyte and differential counts. Note the initial rise in total count, its precipitous fall by the fourth day (toxic inhibition of bone marrow), then its irregular rise and its falling before death (J. E. M.) and before recovery (M. H. P.) to subnormal and normal levels respectively. The per cent of polymorphonuclears generally followed the total count, except toward the end (J. E. M.), when it rose as the total count fell.

On the third day, almost the entire subcutaneous space of the body, particularly the trunk, was greatly distended with fluid. There was no evidence of pulmonary or other complications, and the patient's clinical appearance was good. Laboratory studies at this time showed hematocrit reading, 51 volumes per cent; plasma protein content, 3.91 Gm. per hundred cubic centimeters, with albumin-globulin ratio of 1:1; hemoglobin content, 17.5 Gm.; red blood cell count, 5,350,000, and white blood cell count, 9,800, with polymorphonuclears 86 per cent.

On the seventh day all areas were covered with dressings of isotonic solution of sodium chloride and penicillin solution, 200 units per cubic centimeter, except

the fingers and toes, which were separated by petrolatum gauze. The temperature had been of the remittent type, but now the peaks reached 104 F. (fig. 1). Penicillin was increased to 50,000 units every three hours. The patient was delirious at intervals. At other times he spoke of his impending death with much anxiety. His reasoning was clear, and his predictions were based on what he had read about extensive burns.

The seventeenth day brought a picture of great emaciation and toxicity. The patient looked septic, with drawn, thin, pale face, sunken eyes and dry mouth. He was apprehensive and irritable. The unburned skin was hot and dry. His temperature reached 103 F.; the respiratory and pulse rates were fast. The

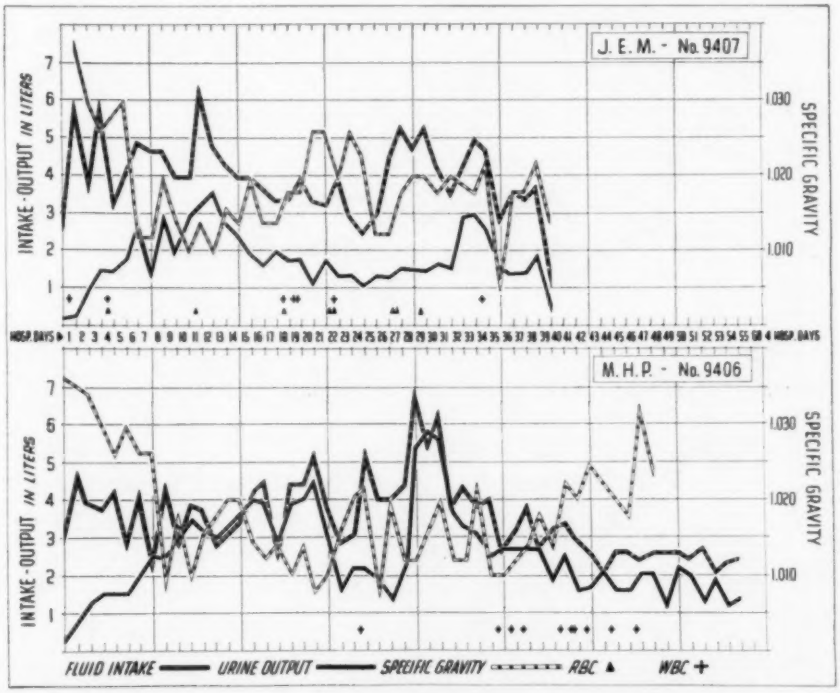

Fig. 3.—Fluid intake by all routes, urinary output, specific gravity and red and white blood corpuscles in the urine. Note the initial anuria, with high specific gravity and blood cell counts despite large intake of fluid. As urinary output increases, specific gravity falls; blood cells are not found. The great variation in specific gravity indicates good renal function but is also dependent on fluid intake and fluid demand. The skin, lungs and gastrointestinal tract take the available interstitial water first (Davis, H. A.: *Proc. Soc. Exper. Biol. & Med.* **43**:354, 1940). The kidneys work with whatever is left over. If the temperature is normal, the skin moist and the amount of urine ample, with the specific gravity not too high, there is enough water and the tubules are conserving a normal amount of water. If, in addition, the sensorium is normal and there is no edema, there is not an overhydration. Since renal function is dependent on osmotic as well as hydrostatis pressure, determination of plasma protein content, with albumin-globulin ratio, is helpful as a guide to treatment. The hematocrit reading, red blood cell count and hemoglobin content are guides in the avoidance of anemia or stagnant anoxia, which may also affect urinary excretion. Note the low urinary output of J. E. M., especially after the seventeenth day, except for four days between the thirty-first and thirty-fifth days.

patient was placed in an oxygen tent. Cold sponges of the face and anterior portion of the trunk were carried out at frequent intervals. The burned areas of the lower part of the legs and feet were treated with packs of 0.5 per cent chloramine-T because they were still infected.

The delirium became worse. He had frequent, involuntary, yellow, semiliquid stools as he lay motionless on his back, refusing all food and water and stating repeatedly that he was going to die. Isotonic solution of sodium chloride was given by hypodermocylsis and, in addition, 1,000 cc. of citrated whole blood intravenously. The burned areas looked good. The necrotic skin had been loosened day by day, and the large areas on the back were now covered with healthy granulations or were entirely healed. There was no visible pus except

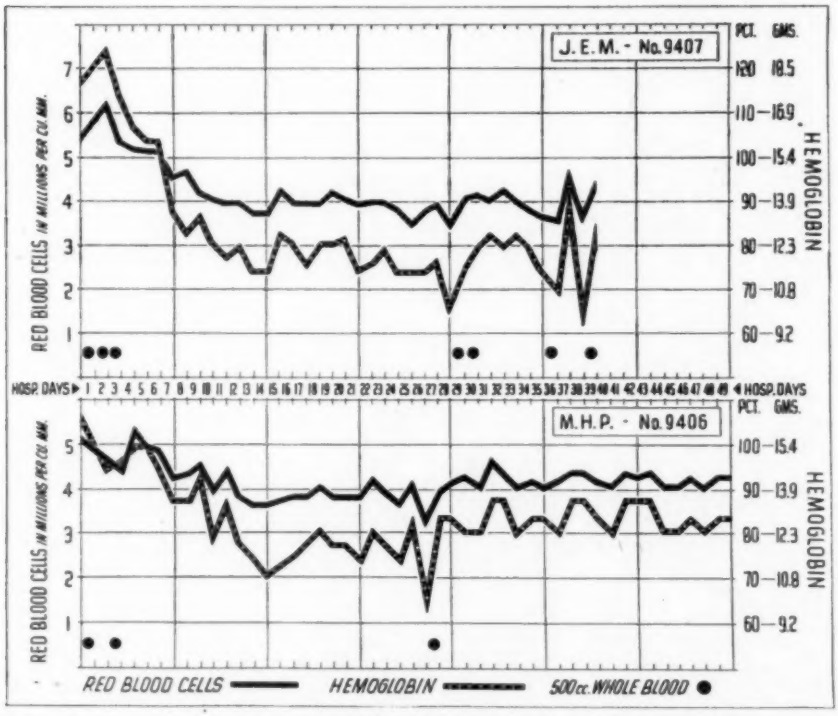

Fig. 4.—Red blood cell count and hemoglobin content are high during the first week because of loss of plasma and water into the burned areas. A more rapid return to normal limits is effected with hypodermoclysis of isotonic solution of sodium chloride and transfusions of whole blood. Patients receiving no specific treatment are also gradually relieved from hemoconcentration by spontaneous hemodilution. J. E. M. had a much higher count (7,200,000) and hemoglobin content (17 Gm., or 112 per cent) than M. H. P.

on some areas of third degree burns of the lower part of the legs and feet. Laboratory studies on the eighteenth day showed: nonprotein nitrogen level, 28 mg. per hundred cubic centimeters; carbon dioxide-combining power, 59.7 volumes per cent; plasma protein content, 4.65 Gm., with 1 Gm. albumin and 3.65 Gm. globulin, per hundred cubic centimeters, and hematocrit reading, 43.5 volumes per cent; leukocytes numbered 16,350, with 83 per cent polymorphonuclears (figs. 2, 3, 4 and 5). Because of low serum albumin content and hematocrit reading, additional

500 cc. units of whole blood and plasma were given on the thirty-fifth and thirty-eighth days. At this time the carbon dioxide-combining power was 102 volumes per cent; erythrocytes, 4,500,000; hemoglobin content, 12.5 Gm.; hematocrit reading, 42 volumes per cent; plasma protein content, 4.4 Gm., with 2 Gm. of albumin, and nonprotein nitrogen level, 27 mg. A persistent, copious diarrhea was present, and the patient had almost continuous, irritating stools. Sulfadiazine, 2.0 Gm., was given every four hours at this time and the buttocks covered with petrolatum gauze. The wounds were clean. The entire back, which was covered with second degree burns, had healed. The thighs were healing rapidly, as were the arms and legs. The face and neck had healed entirely. Urinary output was 1,500 cc. with an intake of 3,500 cc. The urine was acid in spite of a carbon dioxide-

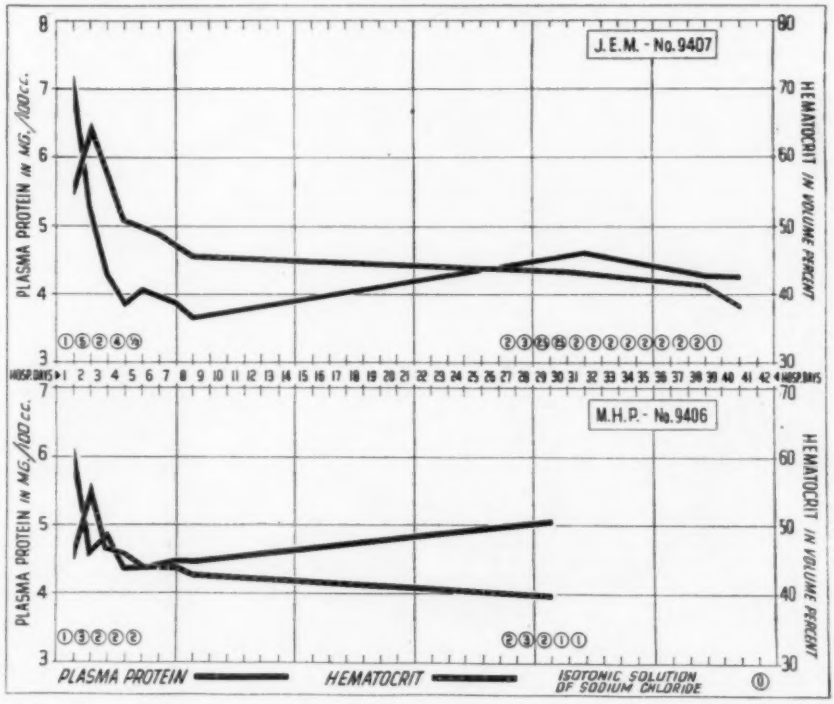

Fig. 5.—Hematocrit reading and plasma protein levels. There is great hemoconcentration during the first forty-eight to seventy-two hours after severe burns. This is due principally to the loss of water and, to a lesser extent, the loss of plasma. Here the plasma protein (chiefly albumin) contents fall rapidly as the hematocrit reading rises. This is quickly controlled with isotonic solution of sodium chloride given in hypodermoclysis into the burned area, which tends to restrict the loss of colloids and crystalloids and augments their reabsorption. Note the fall in hematocrit reading and rise in plasma protein contents as treatment progresses. J. E. M. has more hemoconcentration and slower rise in protein levels than M. H. P.

combining power of 114 volumes per cent. On the thirty-ninth day the patient appeared moribund. Nonprotein nitrogen was 26 mg. The urine was strongly alkaline in reaction. There were muscular twitchings and, later, clonic convulsions. Respirations became labored, and cyanosis was present; the patient became comatose and died on March 28, forty days after admission.

Postmortem Examination.—The significant findings, as described by Dr. H. M. Banks, pathologist, were as follows: The peritoneal cavity contained about 100 cc. of clear, light, yellow fluid; an equal amount of the same type of fluid was present in each side of the chest, and about 35 cc. was found in the pericardium. The cardiac muscle was edematous, with small, scattered accumulations of lymphocytes. There was no pulmonary edema. The spleen was large, weighing 240 Gm. It was engorged with blood. The liver showed extensive fatty infiltration and degeneration. Large areas show total destruction of the parenchymal cells of the liver. The kidneys were swollen, and all their blood vessels were dilated and filled with red blood cells. The tubules showed extensive degeneration and in some areas destruction of the lining cells. The tubules contained refractile droplets as seen in nephrosis. Glomeruli and Bowman's capsule showed little deviation from normal; however, the former were dilated and filled with red blood cells. The cerebrum was edematous. In some areas this was extreme. Here the blood

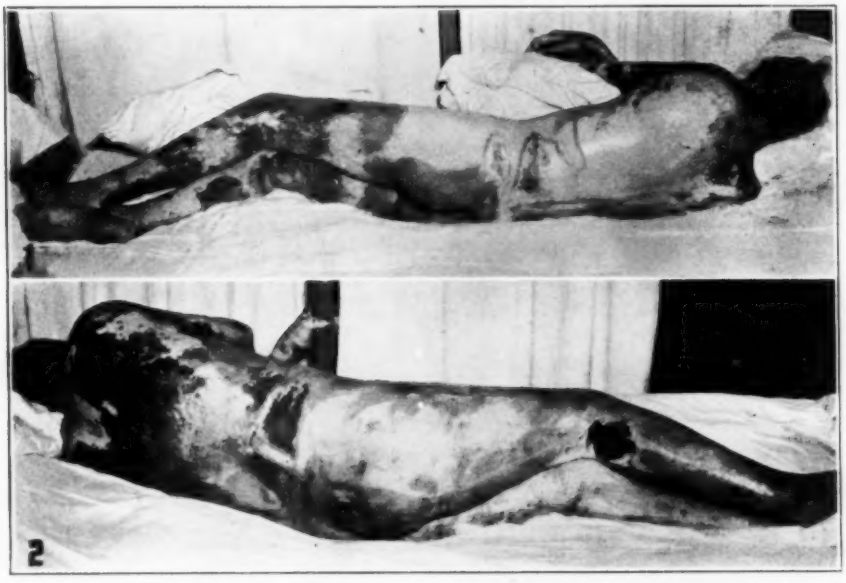

Fig. 6.—*A*, J. E. M. on the eighth day. *B*, M. H. P. on the eighth day.

vessels had shriveled and retracted, and surrounding them there were small areas of advanced autolysis. Ganglion cells were pyknotic and degenerated in such areas. The cerebellum showed practically the same picture as the cerebrum. The adrenals contained areas of fatty degeneration and hemorrhagic extravasation, chiefly in the medullary zone.

Pathologic Diagnosis.—The pathologic diagnosis was (1) edema of cardiac muscle and acute myocarditis; (2) acute peribronchiolar pneumonia, hemorrhagic phase; (3) fatty infiltration of the liver and toxic atrophy of the liver; (4) acute nephrosis and chronic passive congestion of the kidneys, and (5) massive autolysis of the cerebrum, with cerebral edema.

Case 2.—M. H. P., a 43 year old white man, was admitted to the hospital at the same time as J. E. M. He had been burned by the same explosion, over about 71 per cent of his body surface. Although most of the burns were second

degree, the areas involved by third degree were more extensive than in the previous case. The Berkow and Lund-Browder tables being used, the extent and distribution of the burns were estimated to be as follows: head, 2 per cent; neck, 1 per cent; anterior portion of the trunk, 0 per cent; posterior portion of the trunk, 13 per cent; buttocks, 5 per cent; genitalia, 0 per cent; upper part of the arms, 5 per cent; forearms, 6 per cent; hands, 4.5 per cent; thighs, 19 per cent; legs, 13 per cent, and feet, 2.5 per cent. The total equaled 71 per cent of the body surface (fig. 2).

The patient had received exactly the same treatment as J. E. M. prior to his admission to the hospital. He was in severe pain and apprehensive and complained of being cold. His pulse rate was 150 per minute and was thready; the respiratory rate was 30 and the temperature 100 F. orally. The blood pressure was not taken because the cuff could not be applied without great discomfort. Mr. P. was given exactly the same treatment as Mr. M. Laboratory studies showed a hematocrit level of 47 volumes per cent; plasma protein content, 6.15 Gm.; hemoglobin content, 16.5 Gm.; red blood cells, 5,190,000, and white blood cells, 14,300 per cubic millimeter, with 87 per cent polymorphonuclears. Urinalysis showed specific gravity, 1.036; albumin content, 1 Gm. per hundred cubic centimeters, and sugar, 3.8 Gm. per hundred cubic centimeters, with a trace of acetone.

Treatment.—Isotonic solution of sodium chloride was administered by hypodermoclysis into the burned areas, as previously described. Three to 4 liters in twenty-four hours was given. Sodium chloride tablets taken by mouth caused nausea and vomiting, and the administration of them was discontinued. Thirty thousand units of penicillin were given intramuscularly every three hours. Diet and liquids allowed were the same as for J. E. M. Five hundred cubic centimeters of citrated whole blood was given through an ankle vein on the first day, and the injection was repeated on the third day. Laboratory studies, on the third day, revealed a hematocrit reading of 46 volumes per cent; plasma protein content, 4.39 Gm., and albumin-globulin ratio, 1.4:1.0 (figs. 1 to 5). At this time the subcutaneous space of the entire body was greatly distended with isotonic solution of sodium chloride. Its administration was discontinued on the fourth day.

The burns were treated with packs of isotonic solution of sodium chloride, and sloughs were removed carefully each day. Petrolatum gauze was wrapped around the fingers and toes. Butacaine sulfate and merthiolate ointment was used in the eyes for chemical conjunctivitis.

On the eleventh day penicillin was increased to 40,000 units every three hours intramuscularly, because of the persistent fever, which was accompanied with wild delirium. Leukocytes numbered 18,500 per cubic millimeter, with 96 per cent polymorphonuclears. By the sixteenth day the temperature was 99.4 F. orally, and the wounds were clean.

On the nineteenth day the fever returned, and the temperature reached 103 F. orally. The patient was confused. Hallucinations and illusions were interspersed with periods of stupor. The latter were followed by generalized muscular twitchings, which at times became gross clonic and tonic convulsions. There was some cyanosis, and the patient refused food and water. Reflexes were hyperactive. The diagnoses of possible tetany or tetanus or diabetes were considered. Laboratory tests gave the following results: blood chloride content, 561 mg.; blood calcium content, 8.9 Gm.; nonprotein nitrogen level, 26.5 mg.; carbon dioxide–combining power, 30 volumes per cent on March 12, 1946, 47.5 volumes per cent on March 13 and 50.4 volumes per cent on March 16; blood sugar content on March 12 was 204 mg., twelve hours later 135 mg. and on March 13, 190 mg.

At this time hypodermoclysis of isotonic solution of sodium chloride, which had been discontinued on the fourth day, was again started. About 2 liters a day

were absorbed. In addition, the patient was given 500 cc. of whole blood, placed in an oxygen tent and given sodium amytal, 3 grains (0.19 Gm.) intramuscularly as required to control convulsions. Practically all second degree burns had healed. Some third degree burns had healthy granulations and were ready for split thickness grafts. All open wounds were covered with packs of isotonic solution of sodium chloride. Isotonic solution of sodium chloride was injected beneath the burns, sufficient to cause slight weeping. This was repeated once a day. Sloughs were removed each day as they became loose. The injection of isotonic solution of sodium chloride facilitated this greatly.

On the twenty-ninth day the hypodermoclysis of isotonic solution of sodium chloride was again discontinued. The patient was greatly improved. He was given a high protein regular diet and a preparation of vitamin B complex (Becotin [5]) containing thiamine hydrochloride, 3 mg.; riboflavin, 6 mg.; pyridoxine hydrochloride, 1.5 mg.; nicotinamide, 30 mg.; pantothenic acid, 10 mg., and desiccated fraction of liver-stomach concentrate with yeast extract, 0.6 Gm.

The patient was allowed to sit on the side of the bed thirty-seven days after admittance. Skin had to be grafted on some areas, but most wounds healed without excessive scarring, owing to the fact that they were second degree burns.

The patient was released from the hospital fifty-five days after admittance. He was last seen on July 23, 1946, at which time he had entirely recovered.

COMMENT

The treatment of burn shock with hypodermoclysis of isotonic solution of sodium chloride is simple and effective. It is also useful in neutralizing or diluting hypothetic toxins, as illustrated in the case of M. H. P., whose burn toxemia was adequately controlled by this method, and at least partially neutralized in the case of J. E. M. While 2 cases are insufficient to prove any concept, these observations, coupled with the experimental work referred to, form a basis for further study. The patient who died had an alkalosis which may have been due to an excess of sodium. Parenteral administration of fluids (except whole blood) was withheld for forty-eight hours prior to his death; yet the urine remained acid until eight hours ante mortem. The patient took small amounts of water by mouth during this time. Since free fluid was present in the serous cavities, it may seem that too much isotonic solution of sodium chloride was given. A careful review of the case does not bear this out. This is interesting because it illustrates the fact that the fluid will be absorbed from the tissue spaces for osmotic reasons even though the heart is unable to properly propel the absorbed fluid. However, this need not prevent the use of adequate amounts of isotonic solution of sodium chloride by hypodermoclysis, because if the hydrostatic pressure due to cardiac inadequacy exceeds osmotic pressure the sodium chloride given subcutaneously will remain in situ.

A note of warning concerning excessive administration of sodium and fluid should be sounded. Even though the fluid is given subcutaneously or by mouth, we believe that in the late stages of burn

5. Becotin is manufactured by Eli Lilly and Company.

toxemia slight underhydration is safer than overhydration and acidosis is more easily controlled than alkalosis. Our patient (J. E. M.) probably died from toxemia, which was never completely controlled, although practically the same situation was present in the man who recovered (M. H. P.).

At autopsy J. E. M. showed extensive necrosis of the liver and cerebral autolysis. Morphologically, renal changes, such as pigmented casts in the tubules and tubular necrosis, are present in hemolytic reactions to blood transfusion and in burns. Pigment casts were not found in this case, perhaps because the urine was alkaline most of the time.

Burn shock and early burn toxemia may be prevented or adequately controlled by the method outlined. The deciding factor seems to be persistent toxemia, which is probably due to a combination of causes such as dehydration, oligoplasmia, stagnant anoxemia, infection and the absorption of toxins directly from the burned area and secondarily from damage to the liver and kidneys. Most of these integrants may now be successfully dealt with. Infection is still a problem in extensive burns. The best local treatment is to protect the wounds from trauma and let them severely alone, except as already described.[6] Should infection occur, antibiotics (penicillin locally and systemically) and chemotherapeutic agents (sulfadiazine, orally or parenterally) should be used judiciously.

The control of persistent toxemia is a real challenge in burns involving more than 50 per cent of the body surface. Although it may be partially neutralized by sodium, there are still other factors which must be more clearly understood before prolonged burn toxemia can be successfully controlled.

One last problem should be mentioned concerning skin grafting. Had M. H. P. been the victim of third degree burns entirely, then the only available donor site would have been the anterior part of the chest and upper part of the abdomen. Taking skin from this unburned area is hazardous, as it may swing the balance of effects from a 70 per cent burn to one of 100 per cent. Therefore, only small areas could be grafted at any one time.

CONCLUSIONS

1. The use of isotonic solution of sodium chloride by continuous hypodermoclysis into the burned area is strongly recommended in extensive burns for the treatment of burn shock and toxemia.

2. Isotonic solution of sodium chloride by hypodermoclysis is useful during the granulation stage of burn wounds to increase resistance to infection and to stimulate healthy granulation tissue.

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6. Berman, J. K.; Houser, A. D., and Kurtz, W. A.: Wound Immunity, Surg., Gynec. & Obst. **77**:205-208 (Aug.) 1943.

CYSTS OF THE DUODENUM

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CYSTS of the duodenum are rarely reported in the literature. Twelve cases of enterogenous cysts of the duodenum have been described since the initial case of Sänger and Klopp,[1] in 1880. A cyst of the ampulla of Vater, described by Brooks and Weinstein,[2] appears to be one of the mucosa covering the ampulla of Vater, and yet it was both lined and covered with normal duodenal mucous membrane so that, as the authors described, this cyst was a congenital anomaly of the duodenal wall. Microscopic study of this cyst was not reported. These authors were unable to find a similar condition in the literature except the anomalous duodenal pouch presented by Grant,[3] a pouch of mucosa which "hung within the lumen of the gut like a hollow polypus whose mouth was directed towards the pylorus." This pouch showed a reduplication of the entire mucous membrane of the intestine and had the pouch been closed off at its superior margin it would have presented a structure similar to that in the case of Brooks and Weinstein. No Brunner's glands were seen in this pouch. Vogt,[4] in 1925, described a benign perforating duodenal cyst which arose as a retroperitoneal cyst derived from the vestigial remains of the wolffian body and which invaded the duodenum. Vogt considered this to be an endodermal parallel of a teratoma or dermoid cyst, but it represents secondary involvement of the duodenum by extension only. Cysts of Brunner's glands themselves have not been reported as a cause for surgical intervention in duodenal obstruction.

This report is made because of the rarity of duodenal cysts and the occurrence of two of different types within six weeks in the experience of the authors, the two presenting somewhat identical clinical syndromes of intermittent duodenal obstruction, with similar roentgenologic and gross pathologic findings but necessitating different surgical procedures.

From the Gastric Service of the Memorial Hospital for the Treatment of Cancer and Allied Diseases.

1. Cited by Gardner and Hart.[18]

2. Brooks, B. B., and Weinstein, A.: Cyst of Ampulla of Vater, Ann. Surg. **117**:728-734, 1943.

3. Grant, J. C.: Anomalous Duodenal Pouch, Brit. J. Surg. **23**:233-234, 1935.

4. Vogt, M. E.: Benign Perforating Duodenal Cyst Arising from the Vestigial Remains of the Wolffian Body, Am. J. Obst. & Gynec. **10**:798-802, 1925

Collected Cases of Enterogenous Cysts of the Duodenum

Case	Year	Operator	Sex	Age	Symptoms	Physical Examination	Preoperative Diagnosis	Location	Size	Operation	Result
1	1880*	Sänger and Klopp	(?)	Newborn	.....	.....	.....	Three cysts of intestine, 1 arising from accessory bile duct and 1 from accessory liver	"Size of a walnut"	.....	Infant died during difficult labor
2	1881*	Roth	M	Newborn	.....	Abdomen tremendously distended	.....	Large pedunculated cyst arising in third portion of duodenum	.....	Also had enterogenous cyst of mediastinal esophagus	Infant died a few minutes after delivery
3	1919	Meyer	F	3 wk.	Persistent vomiting beginning at 2 wk.	.....	Pyloric stenosis	Cyst extended from pylorus to ampulla of Vater	"Size of a hen's egg"	No operation	.....
4	1922	Waugh	F	19 days	Regurgitation and vomiting	Firm tumor in right side of abdomen	Tumor of right hypochondrium	Large cyst presented on outer side of ascending colon	"Size of a tangerine"	I. Cyst evacuated and packed II. Marsupialization	Died 6 days after second operation
5	1927	Maddox	(?)	3 mo.	Projectile vomiting beginning at 6 wk.	Hard mass in right upper quadrant	Pyloric obstruction (?)	Second portion of duodenum	"Size of a goose egg"	Posterior gastroenterostomy attempted	Died on first hospital day
6	1930	Smith	F	2 wk.	Vomiting	Abdominal distention; palpable tumor questionable	Congenital pyloric stenosis	Cyst of anterior wall of first portion	"Size of a bantam's egg"	Section of wall removed; pylorus dilated; exterior drainage	Died on seventh postoperative day
7	1931	Gardner and Hart	F	15 yr.	Vomiting with attacks of pain	Mass in right upper quadrant	Choledochus cyst	First and second portions of the duodenum	Approximately 10 cm. (?)	Enterocystostomy	Complete recovery
8	1936	Pachman	F	4 mo.	Vomiting	Freely movable mass	Cyst of abdomen	First portion of duodenum; intramuscular	8 by 11 cm.; contents 550 cc.	Partial marsupialization	Died 4 hr. postoperatively
9	1936	Basman	F	4 wk.	Projectile vomiting	Freely movable mass	Pyloric stenosis	Anterior part of first portion	2 to 3 cm. long; contents 15 cc.	I. Evacuation II. Gastroenterostomy 7 days later	Complete recovery
10	1940*	Ladd and Gross	F	5 wk.	Regurgitation and vomiting	Freely movable soft cystic mass above the navel	Omental cyst or enteric cyst	Along mesenteric border of first portion of duodenum	4.5 by 3.5 cm.	Resection of cyst and first portion of duodenum with gastroenterostomy	Protracted recovery
11	1940	Gillespie and Rogers	M	4½ yr.	Jaundice, malaise, abdominal pain, anorexia and abdominal mass of 1 week's duration	Moderate degree of icterus; freely movable globular mass in right upper quadrant	.....	Behind second portion of duodenum, intramuscular	12 cm. in diameter; 350 cc. fluid	Cyst freed; aspirated and discoid mass excised; duodenum closed	Uneventful recovery
12	1941	Orgias	M	2 mo.	Projectile vomiting	Cystic, mobile tumor of right upper quadrant	Renal neoplasm	Pylorus and first portion of duodenum stretched over cyst	3 in. (7.6 cm.) in diameter	Resection with gastroduodenostomy	Uneventful recovery
13	1945	Pack and Booher	M	17 yr.	Intermittent attacks of nausea and vomiting and ptyalism	Fixed mass in right epigastrium	Adenoma (?); myoma (?); cyst of Brunner's gland (?)	Posterior medial wall; first portion extending into second portion	2 cm. in diameter; 8 cc. contents	Enucleation	Complete recovery

* Date reported; other dates indicate year of operation.

AGE AND SEX DISTRIBUTION

There are no data available concerning the age and sex distribution of cysts of Brunner's glands. In Feyrter's [5] case, presenting cystic degeneration of an adenoma, the condition occurred in a man "more than 54 years" of age. Our patient was a man of 52. Of the enterogenous cysts reported, two have occurred in males and eight in females and in 2 cases there was no record as to sex. The ages varied from newborn to 15 years, our 17 year old youth being the third male and the oldest patient recorded.

INCIDENCE

Robertson [6] found 2 instances of cystic dilatation of Brunner's glands in gross examination of 15,000 cases, with microscopic examination in more than 1,000 of them. He cited Rutishauser's presentation of 6 of his own and made a comprehensive review of carcinoma of the duodenum, in which he found 1 case presenting three nodules in the upper portion of the duodenum, which proved to be cysts filled with mucin. Feyrter studied the duodenums of 2,800 patients, in 3 of whom glandular adenomas were found, one of these presenting cystic dilatations containing degenerated cells and masses of mucin. Pack and McNeer [7] collected 16 cases of Brunnerian adenoma from the literature, but none presented evidence of cystic degeneration or retention. Rabinovitch and Pines [8] have found an asymptomatic inclusion cyst of Brunner's gland in the tail of the pancreas in a 42 year old man at necropsy. The cyst wall was made up of a delicate layer of connective tissue lined on the inside by a layer of tall columnar epithelium with a subjacent layer of mucinous glands, which they interpreted as Brunner's glands. Such ectopic origin can be explained on the basis of fetal inclusion, the detachment and independent development of intestinal tissue in some part of the embryo in which it should not occur.

Ackermann [9] reported the incidence of diverticula of the duodenum discovered at autopsy as varying from 3.3 per cent of 1,367 of Lensmayer's cases to 15.5 per cent of Schuppel's cases and an incidence on roentgenologic examination varying from 0.016 per cent of 72,715 examinations by Rankin and Martin to 5.19 per cent of Cryderman's examinations in 770 cases. He found an even higher incidence by making plaster molds of the duodenums of cadavers and found eleven

5. Feyrter, cited by Robertson.[6]

6. Robertson, H. E.: The Pathology of Brunner's Glands, Arch. Path. **31:** 112-130 (Jan.) 1941.

7. Pack, G. T., and McNeer, G.: Unpublished data.

8. Rabinovitch, J., and Pines, B.: Cysts of the Pancreas, Arch. Surg. **45:** 727-746 (Nov.) 1942.

9. Ackermann, W.: Diverticula and Variations of the Duodenum, Ann. Surg. **117:**403-413, 1943.

diverticula in 50 consecutive cases, an incidence of 22 per cent. Yet he made no mention in this series of finding the embryologic counterpart or sequela, that is, an enteric cyst. Pachman,[10] reviewing 36 cases of enterocysts, found 28 cases of cysts in the terminal ileum or ileocecal area as compared with 8 in the duodenum. Ladd and Gross,[11] in 1940, reported 18 patients with cystic lesions situated along various parts of the intestinal canal, which they called "duplications of the alimentary tract," but only one cyst was in the duodenum.

ETIOLOGY AND PATHOLOGY

Robertson's discussion of degeneration and infiltration of Brunner's glands and the resultant pathologic changes is comprehensive:

> The outstanding characteristic of the glands is their comparative freedom from influences which ordinarily affect secreting tissues. General toxemias, starvation states and dietary deficiencies apparently leave them unscathed. The cells at times have an almost clear cytoplasmic content, staining only faintly or not at all with ordinary dyes or even with specific mucin stains, and the ducts are free from stainable substances. This condition has been pointed out as evidence of increased function, but I have observed it in the region of duodenal ulcers and other inflammatory processes in the mucosa of the duodenum. Occasionally there is stasis of secretion, with dilated ducts and acini. In some cases this is evidently because of obstruction to the ducts; it has been observed in the region of invading or metastatic tumor nodules and on the margins of chronic or healed ulcers. Such a condition may lead to cyst formation, in which acini or even an entire lobule may be dilated and contain a mass of cell detritus mixed with varying amounts of mucin. . . . More rarely occur large cysts reaching several millimeters in diameter and producing easily observable nodules in the duodenal wall. . . . These cysts are lined with low cuboid cells, and the lumens are largely free from stainable substances.

Hartz and van der Sar,[12] contrary to Robertson, concluded that in the presence of inflammatory conditions the epithelium of Brunner's glands reacts in the same way as glandular epithelium in other parts of the body. With this viewpoint it is even more surprising that evidence of hypersecretion and subsequent retention is not observed more frequently, when one considers the many and variable stimuli the duodenal mucosa receives.

Information as to the position in the duodenum and the size of cysts of Brunner's gland is lacking. Robertson stated that the size varies from the dilatation of a lobule to cysts several millimeters in diameter. Feyrter's adenomas ranged from the size of a pea to that

10. Pachman, D. J.: Enterogenous Intramural Cysts of the Intestines, Am. J. Dis. Child. **58**:485-505 (Sept.) 1939.

11. Ladd, W. E., and Gross, R. E.: Surgical Treatment of Duplications of the Alimentary Tract, Surg., Gynec. & Obst. **70**:295-307, 1940.

12. Hartz, P. H., and van der Sar, A.: Proliferative Activity in Brunner's Glands, Am. J. Path. **20**:931-943, 1944.

of a hazelnut, but the size of the cyst is not given. Our patient presented a cyst 1.5 by 2 cm. occurring on the anterior wall of the duodenum.

There are several theories concerning the causation of enterogenous cysts. Lewis and Thyng,[13] in a review of the occurrence of intestinal diverticula in embryos of the pig, the rabbit and man, concluded that "knoblike" intestinal diverticula occur regularly in these embryos, and their presence was noted in the cat and the sheep. The authors were of the opinion that these "knoblike" diverticula were the probable source of an occasional accessory pancreas and that they usually degenerated, sometimes forming detached cysts and nodules. It was felt that these structures might give rise to pathologic diverticula. Ewing[14] concurred that they might arise from misplaced portions of the intestine and stated that Beneke had designated cysts of this origin as "entodermoid."

It does not seem likely that enteric cysts arising as far cephalad as the duodenum should arise from Meckel's diverticulum or the vitello-mesenteric duct, which is a possible source of origin for those of the ileomesenteric area. Orgias[15] concluded that the cyst in his case "is a developmental cyst of the duodenum and has developed as a diverticulum of the first part of the duodenum." Evans,[16] in reviewing both enterogenous cysts and diverticula of the intestine, stated: "There can be no doubt that cysts whose walls reproduce completely or incompletely the structure of gut, whether discovered in the wall of the gut, attached to the gut, or even more or less remote from the gut, must have been derived from gut. They are developmental cysts."

Hughes-Jones[17] proposed a theory of epithelial sequestration as a possible origin of enterogenous cysts. He made serial sections of a number of human embryos and in 2 found evidence of epithelial sequestration. In 1 a small cyst was lined by epithelium resembling that of the adjacent bowel. Hughes-Jones felt that these islets were separated before the circular musculature was formed and that after they were formed the isolated epithelium gained its muscle coat by a condensation of the undifferentiated mesenchyme surrounding the intestine.

If these "knoblike" diverticula or misplaced or displaced enteric anlages are the source of origin for both cysts and diverticula, it is

13. Lewis, F. W., and Thyng, L.: The Regular Occurrence of Intestinal Diverticula in Embryos of the Pig, Rabbit and Man, Am. J. Anat. **7**:505-519, 1907.

14. Ewing, J.: Neoplastic Diseases, ed. 4, Philadelphia, W. B. Saunders Company, 1940, pp. 1062-1063.

15. Orgias, R.: Enterogenous Cyst, Brit. J. Surg. **31**:90-93, 1943.

16. Evans, A.: Enterogenous Cysts and Diverticula, Brit. J. Surg. **17**:34-83, 1929.

17. Hughes-Jones, W. E. A.: Enterogenous Cysts, Brit. J. Surg. **22**:134-141, 1934.

surprising that primary diverticula of the duodenum are so frequent and cysts so uncommon if they are in reality different phases of the same process.

Enterogenous cysts may occur anywhere in the wall of the bowel or in the mesentery and are classified as submucosal, intramuscular, subperitoneal and intramesenteric. They have occurred most frequently in the second portion of the duodenum but have extended up to the pylorus and have arisen behind the first portion. The size has varied from the size of a walnut to cysts containing 500 cc. of fluid. The average size has been approximately 6 to 7 cm. in diameter.

By definition, the walls of these cysts correspond to the structure of the intestinal canal. They present well defined muscular coats and glandular linings, and, although intracystic pressure may cause atrophy and flattening of the glands, the glands of Brunner are apparent.

SYMPTOMS AND FINDINGS

Except for the patients in the first 2 reported cases, the cysts in whom were discovered at autopsy, all patients with enterogenous cysts have presented signs and symptoms of duodenal obstruction, so that a diagnosis of pyloric stenosis was entertained in cases of infants. Persistent vomiting or regurgitation has been the predominant symptom, twice occurring with pain. In 9 of the 12 cases of enterogenous cysts previously reported a tumor had been palpable. In only 1 of our cases, that of the enteric cyst, was a mass palpable. The most important diagnostic signs noted by Gardner and Hart [18] were palpable tumor and signs of duodenal obstruction. Pachman's analysis of symptoms and findings in his report of 8 cases of intramural cysts is most complete, and any one having unusual interest in this subject is referred to his comprehensive review of enterogenous cysts. Ladd and Gross observed that most cysts of the duodenum, jejunum and ileum brought early signs of intestinal obstruction, characterized by colic-like pain, vomiting, increased peristalsis and, finally, signs relating to dehydration. Hemorrhage due to interference with intestinal blood supply has not occurred in the duodenal lesions, unless the unexplained hematemesis occurring at the age of 6 months in the patient of Gardner and Hart was due to the cyst which was operated on fourteen years later, though there had been no continuity of symptoms. In only the case of Gillespie and Rogers [19] was there evidence of biliary obstruction. Since

18. Gardner, C. E., Jr., and Hart, D.: Enterogenous Cysts of Duodenum: Report of a Case and Review of the Literature, J. A. M. A. **104**:1809-1812 (May 18) 1935.

19. Gillespie, J. B., and Rogers, J. C.: Enterogenous Cysts of the Duodenum. Arch. Pediat. **57**:652-658, 1940.

only two of the previously reported cysts were in patients over 4 months of age, it appears that these lesions, if they occur in the duodenum, produce symptoms early and that the cysts have little opportunity to attain great size.

Cysts of Brunner's glands are usually asymptomatic.

ROENTGENOLOGIC DIAGNOSIS

In the case of Ladd and Gross there was sufficient compression of the first and second portions of the duodenum to give evidence of partial obstruction. In the case of Pachman there were no findings on gastrointestinal examination to suggest obstruction, though the infant presented peristaltic waves and was vomiting at the time. The case of Gardner and Hart presented no apparent anomaly on gastrointestinal roentgenologic study. Our roentgenologic findings have been similar and definite. Both patients have presented a round central filling defect of the second portion of the duodenum, but there has been nothing characteristic to differentiate it from papilloma or polypoid benign tumor of the wall.

TREATMENT

Four methods of surgical approach are possible: (1) duodenal resection with the adjacent cyst, (2) enucleation or excision, (3) simple evacuation and (4) marsupialization.

Of the 12 cases of enterogenous cysts reported to date, there have been 5 cases of recovery following surgical removal. The first reported cyst, of Sänger and Klopp, in 1880, was discovered at autopsy in an infant who died during a difficult delivery. The patient of Roth,[18] in 1881, died a few minutes after delivery, and in the case of Meyer,[19] reported in 1919, a diagnosis of pyloric stenosis was made, but the patient died without surgical intervention. Waugh,[20] in 1923, apparently was the first to operate on an enterogenous cyst of the duodenum. His patient was a 19 day old girl and he found a retroperitoneal cyst which was adherent to the posterior wall of the duodenum. He packed the cavity of the cyst with gauze, but six weeks after the removal of the gauze it refilled. Six weeks later the child was operated on again, the cyst wall being sutured to the aponeurosis of the abdominal wall, but the child died of pneumonia six days after the second procedure. Posterior gastroenterostomy was attempted for Maddox'[21] patient, but the condition of the child made it impossible to complete the operation.

20. Waugh, O. S.: Congenital Cyst of the Duodenum, Surg., Gynec. & Obst. **37**:785-787, 1923.

21. Maddox, K.: Cyst of the Duodenum Simulating Pyloric Obstruction, M. J. Australia **1**:900, 1927.

The child died the day of the operation. Smith,[22] in 1930, operating on a 2 week old infant with a cyst of the anterior wall of the duodenum, drained it externally. The child died one week postoperatively, the cyst having regressed greatly in size. The first successful operation was that of Gardner and Hart, in 1929, who treated a 15 year old girl by anastomosing the cyst to the intestinal tract. In Basman's [23] case, reported in 1938, of a 4 week old child presenting signs of pyloric stenosis, evacuation of the cyst alone was done because of the poor condition of the infant, but in seven days the tumor was again palpable and the abdomen was reopened, showing that the cyst had refilled. An attempt was made to enucleate the cyst, but when the operator failed to find a line of cleavage a gastroenterostomy was performed.

In Pachman's case, after 550 cc. of greenish black thin fluid had been aspirated, a small portion of cyst wall was removed for biopsy and a small catheter was inserted and secured to the peritoneal opening to effect partial marsupialization. The infant died four hours after operation. Ladd and Gross resected the first portion of the duodenum and performed a posterior gastrojejunostomy. Gillespie and Rogers aspirated 350 cc. of the contained fluid from their patient and then excised the collapsed discoid sac and inverted the duodenal wall. This presented a technical difficulty insofar as the medial wall of the excision was adjacent to the common bile duct, but when the duct was probed before the abdomen was closed it showed no obstruction. In the last case reported, Orgias attempted to dissect the cyst off the posterior portion of the pylorus and the first portion of the duodenum but, finding it impossible, resected the involved portion of the stomach and duodenum with subsequent end to end anastomosis, with an uneventful recovery.

In our case an intramural enterogenous cyst was enucleated, as was attempted in the cases of Basman and Orgias, and though a good line of cleavage was not possible it was shelled out by both sharp and blunt dissection and the muscular and mucosal layers closed separately.

Ladd and Gross stated that the treatment of enterogenous cysts consists in complete excision, with removal of the attached portion of the alimentary tract. They recommend this because their experience has shown that the masses cannot be enucleated without danger of perforating the viscus or leaving it in an ischemic state. We concur with this even after successful enucleation in our case. The feeling that our second case presented similar findings to our first case, in

22. Smith, R. E.: A Case of Enterocystoma of the Duodenum Simulating Congenital Pyloric Stenosis, Guy's Hosp. Rep. **80**:463-465, 1930.

23. Basman, J.: Enterogenous Cyst of the Duodenum Simulating Pyloric Stenosis: Report of a Case in an Infant with Recovery Following Gastroenterostomy, J. Pediat. **12**:363-366, 1938.

which the mass enucleated so easily, caused us to pursue the procedure once it was undertaken, even though difficulty became apparent. Examination of the wall revealed no perforation of the muscularis and good color of the entire duodenal wall, so that the procedure was concluded at this stage. However, the fear of jeopardizing the viability of bowel wall by enucleation may be more theoretic than actual insofar as Miller [24] recorded 10 cases of enucleation in the ileocecal region, without a death.

Of the 6 survivors in the 13 collected cases, 2 have had resection of the adjacent duodenum, gastrointestinal continuity being reestablished by gastrojejunostomy and gastroduodenostomy once each. One patient had a gastrojejunostomy after drainage of the cyst, and 1 had only an enterocystostomy, a remarkably successful form of uncomplicated evacuation. Two instances of local excision with successful results are recorded. This represents an operative mortality of 45.4 per cent and a case mortality rate of 53.8 per cent.

Enucleation of the cysts of Brunner's glands is not attended with the difficulties inherent in management of the enterogenous cyst. Simple enucleation is sufficient for this problem, which presents grossly similar findings.

REPORT OF CASES

CASE 1.—E. A., a 52 year old white man, was first seen on July 24, 1945, complaining of loss of weight, anorexia and fatigue of three months' duration. He had occasional abdominal cramps, which he attributed to constipation. He had never observed melena or clay-colored stools.

General physical examination revealed a normally proportioned man, weighing 150 pounds (68 Kg.), who presented no evidence of jaundice but appeared anemic. He had no cervical adenopathy, and the thyroid gland was not enlarged. The heart, lungs and blood pressure were normal. Examination of the abdomen revealed no tenderness in the epigastrium or over the duodenum. No masses were palpable, and the liver and spleen could not be palpated. Results of urinalysis were entirely normal, and the red blood cell count was 3,670,000, hemoglobin 79 per cent, or 11.5 Gm. per hundred cubic centimeters by the Sahli method, and the white blood cell count 12,000, with polymorphonuclears 65 per cent, lymphocytes 32 per cent, monocytes 2 per cent and eosinophils 1 per cent.

The submitted report of roentgenographic examination by Dr. Maurice Rona showed a normal chest except for a large ossified primary focus of primary tuberculosis infection in the middle lobe of the right lung, which was deemed entirely inactive. A series of roentgenograms of the gastrointestinal region, taken on July 10, was reported as follows: The stomach is medium in size and normal in position, shape, outline, tone and peristaltic contraction, filling smoothly in all its parts, without evidence of organic changes. The pyloric valve shows a tendency toward spasm. The bulb is small to medium in size and somewhat flattened in shape but without evidence of organic defects. The second portion of the duodenum fills out normally, but at the region of the papilla of Vater an oval-

24. Miller, R. T.: Enterogenous Mesenteric Cysts, Bull. Johns Hopkins Hosp. **24**:316-322, 1913.

shaped filling defect 1.5 cm. in width is constantly present and suggests a tumefaction arising from the papilla. The loop of the duodenum is apparently widened, but no evidence of pressure and no change in the mucosal outline are seen. The jejunum and ileum show some scattering of barium but no gross abnormalities. The motility of the stomach and of the small intestines is normal.

Résumé.—The findings in the gastrointestinal tract may be regarded as normal except for the tumefaction in the descending duodenum. The nature of the tumefaction cannot be determined from the roentgenograms alone.

Cholecystograms revealed a normally functioning and noncalculous gallbladder.

The presumptive diagnosis was papillary tumor of the duodenum. Laparotomy and removal of the duodenal polyp by the transduodenal route were recommended.

Fig. 1 (case 1).—In this roentgenogram the second portion of the duodenum fills out normally, but at the region of the papilla of Vater an oval-shaped filling defect 1.5 cm. in width is present. It suggests a tumefaction arising from the papilla of Vater.

The patient was admitted to the Memorial Hospital for the Treatment of Cancer and Allied Diseases on July 30, 1945, and laparotomy was performed the following day. A right paramedian celiotomy was done, and, on palpation of the second portion of the duodenum, a smooth cystic mass measuring 1.5 by 2 cm. was palpated on the anterior wall of the second portion, extending to the left wall. A transverse incision was made over the mass in the second portion of the duodenum, and the cyst was seen to be covered entirely by mucosa and seemed

to be within the mucosa itself. It was well encapsulated and contained white mucoid fluid. The cyst was opened and evacuated and a careful dissection carried out, the capsule being removed. The duodenal mucosa was repaired, and at completion of this stage the gallbladder was compressed and the flow of bile indicated free evacuation of the gallbladder. The duodenal wall was then closed in three layers and the incision closed in layers, with drainage to the site of duodenal closure.

The postoperative course was complicated by localized peritonitis, which responded to penicillin therapy. The patient was entirely asymptomatic by the fourth postoperative day and was discharged on the fifteenth postoperative day.

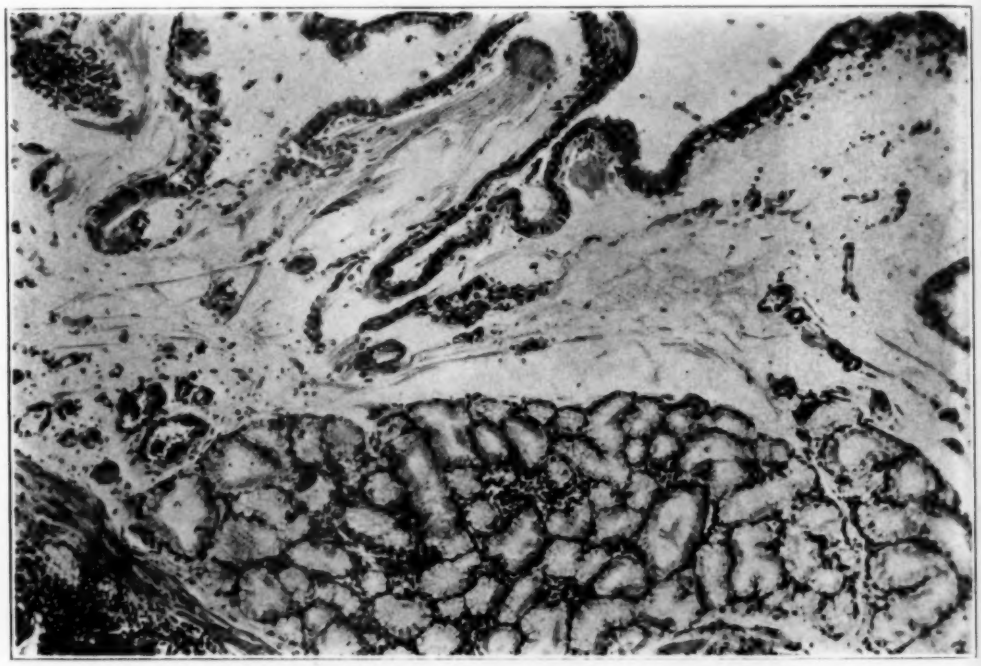

Fig. 2 (case 1).—Photomicrograph showing that beneath a moderately attenuated duodenal mucosa are multiple cystic spaces which arise in glands or ducts of Brunner's glands. In many of these foci the lining epithelium is of characteristic type, but in other areas it is cuboidal.

Pathologic Examination.—The specimen consists of a small sac; one area is covered by mucosa and the remaining two thirds by roughened, frayed, muscular tissue. The wall is approximately 0.4 mm. thick.

Microscopic Examination.—Beneath a slightly to moderately attenuated duodenal mucosa are multiple cystic spaces, which obviously have their origin in glands or ducts of Brunner's glands. In many of these foci the lining epithelium is of characteristic type, but in some areas the lining cells become cuboidal and somewhat more opaque. Here and there are scattered and inconspicuous uniradicular papillary excrescences, but in general the cystic spaces have a single epithelial lining. The largest of the cystic spaces is about 1.5 mm., but larger

spaces may have been disrupted prior to receipt of the specimen. Sections do not include muscularis.

Diagnosis.—The diagnosis was multiple cysts of Brunner's glands.

CASE 2.—I. B., a 17 year old white student, was referred from the medical clinic of Dr. Lloyd F. Craver at the Memorial Hospital for the Treatment of Cancer and Allied Diseases on June 22, 1945. He complained of vomiting early in the morning occurring about twice monthly since he was 12 years old. The usual sequence of these periodic bouts of vomiting was ptyalism, early morning nausea and epigastric pain which would be constant for periods of two to three minutes and then subside, to return again in about fifteen minutes. The whole attack would last about one hour, but the sense of nausea would usually persist through the day. These attacks were associated with nervous tension and were not associated with food intake. About a year after the symptoms appeared his family doctor was consulted, and a series of roentgenograms of the gastrointestinal tract was made and the patient told that there was "a scratch in the wall of the stomach." He was placed on a diet, which he followed with little constancy, and the vomiting spells continued to occur once or twice a month. Approximately eight months before the patient had come to the Memorial Hospital for the Treatment of Cancer and Allied Diseases, another doctor had taken a series of roentgenograms of the gastrointestinal region and had told the patient that he had a benign tumor. The patient was again placed on a diet, and the vomiting spells ceased but nausea continued in the early morning and, occasionally, epigastric pain. His appetite was poor, but he had daily bowel movements and had no other gastrointestinal complaints. The month before admission his local draft board had classified him as 4F because roentgenographic studies revealed "some pathology in the stomach." The only significant item in his past history was an uncomplicated bilateral mastoidectomy at the age of 4. He used both alcohol and tobacco occasionally, and his family history presented no history of carcinoma, tuberculosis or diabetes.

Physical examination revealed a slightly undernourished and sallow boy, weighing 123 pounds (55.8 Kg.). The lungs, heart and blood pressure were apparently normal. There was tenderness in the right paraumbilical region, and a small fixed mass could be palpated just to the right of the spinal column, slightly above the umbilicus. The liver, spleen and kidneys were not palpable, and no abdominal, iliac or inguinal nodes could be felt. The laboratory studies revealed hemoglobin of 95 per cent, 4,400,000 red blood cells per cubic centimeter and a white blood cell count of 9,300, with 59 per cent polymorphonuclear filamented forms, 6 monocytes and 35 per cent lymphocytes. Results of urinalysis were normal except for an occasional red blood cell.

Roentgenologic studies of the gastrointestinal tract on July 6, 1945 were reported by Dr. Ruth Snyder, as follows: On fluoroscopy, the esophagus canalized normally. The stomach showed no intrinsic disease; there was good peristalsis and emptying. The duodenal cap showed a deformity, with a concavity on the side of the greater curvature. This was constant and apparently due to a tumor within its walls in this location. The roentgenograms showed a deformity of the duodenal cap similar to that seen on submitted roentgenograms (dated Feb. 19, 1940 and Dec. 2, 1944), and the appearance suggests a fairly large tumor of the wall of the cap on the side of its greater curvature. This may be due to a polyp or myoma or similar process. It is not obstructing, and the stomach was almost emptied at one hour.

The patient was then admitted to the hospital, on July 7, 1945, and additional spot roentgenograms of the duodenal cap showed no change in the defect in the midportion and distal portion of the cap. Gastric analysis showed no blood or bile, with 100 degrees of free hydrochloric acid and 106 degrees of total acidity and, on repetition, 47 degrees of free hydrochloric acid and 53 degrees of total acidity. Stool specimens showed no occult blood.

The presumptive diagnosis was benign tumor of the duodenum, either myoma or adenoma, though one member of the staff was influenced by the preceding case and made a diagnosis of duodenal cyst.

Fig. 3 (case 2).—The roentgenogram of the duodenal cap shows a deformity, with a concavity on the greater curvature side. The appearance suggests a fairly large tumor of the wall of the cap on its greater curvature side.

On September 10 exploratory laparotomy was done through a midline incision in the upper part of the abdomen. On palpation of the first portion of the duodenum and just beyond the pylorus and extending into the second portion of the duodenum, a firm, tense mass was palpated. On palpation it could be separated from the head of the pancreas. The anterior wall of the duodenum was easily movable over it. Palpation of the liver revealed no cysts, and palpation of the right kidney was noncontributory. The second portion of the duodenum was mobilized by Kocher's maneuver. A longitudinal incision was made in the anterior wall of the duodenum, beginning 2 cm. distal to the pylorus and

extending to the papilla of Vater. This exposed the tumor of the posteromedial wall of the duodenum. The mucosa was freely movable over it. A needle was introduced into the cyst, and 8 cc. of clear slightly mucilaginous fluid was obtained. Incision was then made through the mucosa, and the wall of the cyst was identified. With blunt dissection the wall of the cyst was separated from the mucosa, though the wall of the cyst was ruptured during the procedure. The cystic capsule was removed by a combination of blunt and sharp dissection and the muscular wall sutured with a running suture to control oozing from this area. The mucosa was closed to effect complete hemostasis. The anterior duodenal wall was closed in a transverse direction with a Connell inverting suture and a seromuscular continuous locked suture of silk. An

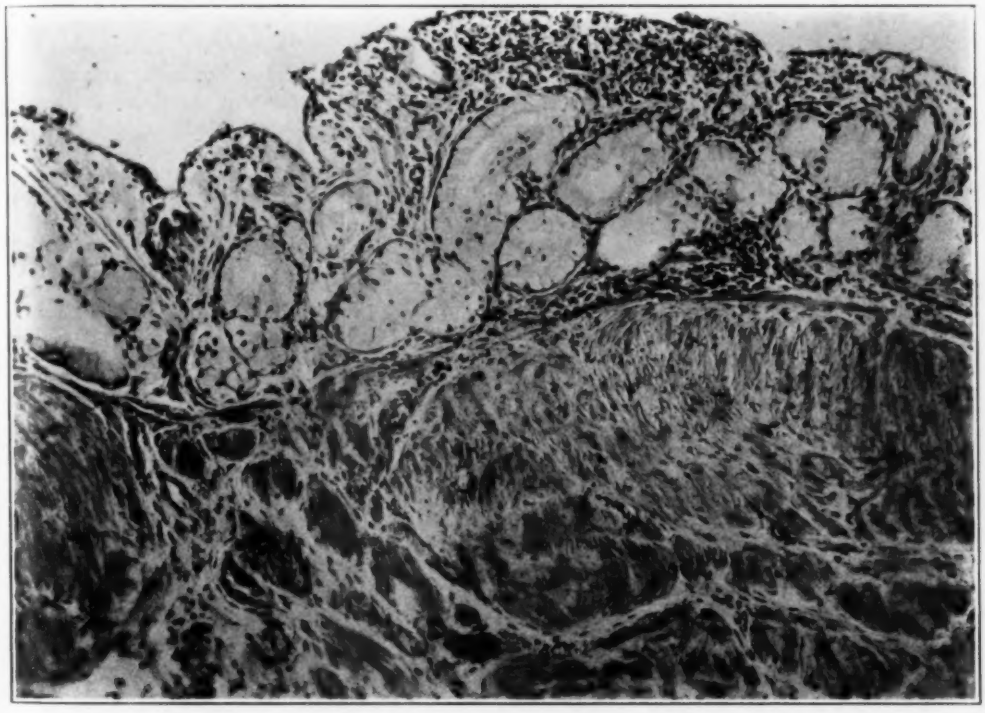

Fig. 4 (case 2).—The photomicrograph presents the internal margin of the cyst wall. The circular and longitudinal muscular coats are about one-fourth to one-third normal thickness. Brunner's glands are reduced in mass and number. There is moderate interstitial fibrosis and round cell infiltrate. The atrophic duodenal mucosa is not included in the section.

indwelling Levine tube was then guided into the third portion of the duodenum. The abdominal wall was closed in layers with silk and reenforced with retention sutures, with one cigaret drain placed over Morrison's pouch.

One transfusion of 500 cc. was given on the third day, though the blood count was essentially unchanged from the first count. The hospital course was uneventful, the drain being completely removed by the fifth day, the last sutures out by the twelfth and the patient home on the twelfth postoperative day. The patient has been seen in the clinic since that time, and for the first six weeks

after leaving the hospital he had occasional periods of nausea in the early morning. A series of roentgenograms of the gastrointestinal region on October 23 showed a postoperative deformity of the duodenal bulb but no obstruction in the first and second portions of the duodenum. Since that time the patient has been asymptomatic and is back to employment in a new field, as a dental technician, free of all symptoms, having gained 3 pounds (1.3 Kg.).

Pathologic Examination.—The specimen consists of a small cyst, with a diameter of approximately 2 cm. Part of the wall consists of frayed muscular tissue. The interior of the cyst is smooth and presents no unusual gross chracteristics.

Microscopic Examination.—There is almost complete atrophy of the duodenal mucosa; there is only a single epithelial layer, which is variously columnar to low cuboidal. The lamina muscularis mucosa is scarcely recognizable, being reduced to a filamentous membrane. The circular and longitudinal muscular coats are about one fourth to one third of the normal thickness. Brunner's glands are greatly reduced in mass and are entirely absent in multiple areas. There is moderate interstitial fibrosis accompanied with a fairly dense round cell infiltrate. This is most prominent in the areas of Brunner's glands but involves the entire muscular wall in some areas.

Diagnosis.—The lesion represents a form of congenital cystic dilatation of the duodenum.

SUMMARY

1. The problem of duodenal cysts has been reviewed.

2. A case of cystic dilatation of Brunner's glands is recorded, the first necessitating surgical intervention for duodenal obstruction.

3. The thirteenth case of a patient with an enterogenous cyst of the duodenum is recorded, the sixth patient who has survived operation. The operative mortality rate for these collected cases is 45.4 per cent.

4. The surgical management of these cystic lesions has been discussed.

5. Simple enucleation of the cysts, with reconstruction of the wall and transverse closure of a duodenotomy in the longitudinal plane, has relieved the symptoms of obstruction in these 2 patients.

6. Simple enucleation is adequate treatment for cysts of Brunner's glands, but this procedure applied to an enterogenous cyst may be attended with injury to the duodenal wall.